EXHIBIT 10

DECLARATION OF MARK DERSHWITZ, M.D., Ph.D.

1. I am a medical doctor with a Ph. D. in Pharmacology. A true and accurate copy of my curriculum vitae is attached as Exhibit A. I am licensed to practice medicine in the states of Massachusetts and Maine. I am currently an anesthesiologist at the University of Massachusetts and I am certified by the American Board of Anesthesiology. I am currently Professor of Anesthesiology and Biochemistry & Molecular Pharmacology at the University of Massachusetts.

2. I have done extensive research and written numerous review articles and research papers on the use of anesthetics and I regularly practice medicine in that capacity. My research includes the study of pharmacodynamics and the pharmacokinetics of drugs. Pharmacokinetics is the study of the time course of a drug, while pharmacodynamics refers to the effects of a drug. Prior to my current appointment at the University of Massachusetts, I was an Instructor, Assistant Professor and Associate Professor at Harvard Medical School.

3. I have testified as an expert witness concerning the pharmacokinetics and the pharmacodynamics of anesthetic drugs and other medications. I have testified in court as an expert witness on seventeen occasions. I have given thirty-six depositions as an expert witness.

4. I have reviewed the protocols for the lethal injections used in the states of Arkansas, Alabama, California, Florida, Georgia, Kentucky, Maryland, Missouri, Montana, North Carolina, Ohio, Oklahoma, South Carolina, Texas and Virginia and by the federal government. In addition, I have reviewed the document from

EXHIBIT 10

the State of Washington Department of Corrections entitled, "Capital Punishment," and numbered "DOC 490.200." Each of the states and the federal government employ similar protocols for carrying out lethal injections. While the protocols and the jurisdictions differ in terms of the doses of the three medications used, each of these protocols will render an inmate unconscious quickly and cause the inmate's rapid and painless death.

5. Some medical paraprofessionals, such as nurses, emergency medical technicians, and paramedics, may be trained to insert intravenous catheters. If a medical paraprofessional routinely inserts intravenous catheters as a part of his or her regular job, it is reasonable to assign the task of inserting the intravenous catheter in an inmate to this person.

6. The protocol used in Washington states that medications will be administered as follows:

a Thiopental sodium, 3 grams, will be injected.

b. Saline, 50 mL, will be injected to flush the IV line.

c. The Superintendent will observe the inmate for signs of consciousness. If the Superintendent observes that the inmate is conscious, an additional dose of thiopental sodium, 3 grams, will be injected.

d. Pancuronium bromide, 100 mg, will be injected.

e. Saline, 50 mL, will be injected to flush the IV line.

f. Potassium chloride, 240 mEq, will be injected.

g. The superintendent will direct the physician on site to examine the inmate

and pronounce death.

7. I have performed a pharmacodynamic analysis to predict the probability of response as a function of the predicted brain concentration of thiopental. This analysis is attached as Exhibit B. There are two responses to thiopental depicted in Exhibit B. The first response is the probability of unconsciousness. In this context, unconsciousness is defined as the drug-induced inability to perform a simple command such as "raise your right arm." An unconscious person is unable to perceive his or her environment. The second response is the probability of burst suppression. Burst suppression is a state of the brain as measured by an electroencephalograph (EEG) in which the EEG demonstrates the periodic absence of electrical activity. This state is readily demonstrable during the administration of clinical anesthesia for surgical procedures by using available clinical monitors. While burst suppression is easy to measure, it is a state of anesthesia that is deeper than that required for the performance of surgery.

8. I have performed a pharmacokinetic analysis to predict the brain concentration of thiopental in a man weighing 106 kg following the administration of a 3-gram dose of thiopental sodium. I assumed that the thiopental solution was injected at a rate of 50 mg/sec (50 milligrams per second). My pharmacokinetic analysis is attached as Exhibit C. This pharmacokinetic graph shows the predicted concentration of thiopental in the brain of a 106-kg man as a function of time following a dose of 3 grams. The y-axis is the predicted concentration of

thiopental in the brain measured in mcg/mL (micrograms per milliliter). The x-axis is time in minutes. As shown in Exhibit C, after the administration of 3 grams of thiopental sodium, the brain concentration of thiopental would peak at a concentration of about 84 mcg/mL about 3.5 minutes after beginning the injection.

9. The lower dashed line in Exhibit C indicates the brain concentration at which there is an approximately 95% probability of unconsciousness. This predicted concentration is exceeded for more than an hour following the beginning of the injection, assuming that the inmate continued to breathe.

10. The upper dashed line in Exhibit C indicates the brain concentration at which there is an approximately 95% probability of burst suppression. This predicted concentration is exceeded for approximately ten minutes following the beginning of the injection, assuming that the inmate continued to breathe.

11. A dose of 3 grams of thiopental sodium will cause virtually all persons to stop breathing. Thus, although the subsequent administration of pancuronium bromide, a paralytic agent, would have the effect of paralyzing the person and preventing him or her from being able to breathe, virtually every person given 3 grams of thiopental sodium will have stopped breathing prior to the administration of pancuronium bromide. Thus, even in the absence of the administration of pancuronium bromide and potassium chloride, the administration of 3 grams of thiopental sodium by itself would cause death to almost everyone.

12. I have co-authored a recently published article discussing in much greater detail the pharmacology of the medications used in lethal injection. This article is appended as Exhibit D.

13. Therefore, it is my opinion to a reasonable degree of medical certainty that there is an exceedingly small risk that a condemned inmate to whom 3 grams of thiopental sodium is properly administered pursuant to the lethal injection protocol of the State of Washington would experience any pain and suffering associated with the administration of lethal does of pancuronium bromide and potassium chloride.

14. It is my opinion to a reasonable degree of medical certainty, the proper application of the of the State of Washington lethal injection protocol will result in the condemned inmate undergoing a rapid, painless and humane death, and furthermore, the inmate will not experience any unnecessary pain or suffering.

I declare under the penalty of perjury that the foregoing is true and correct.

Executed on November 3, 2008

By /Mark Dershwitz MD/
Mark Dershwitz, M.D., Ph.D.

EXHIBIT A

CURRICULUM VITAE

(prepared 3 November 2008)

NAME: Mark Dershwitz

ADDRESS: 33 Wildwood Drive
Sherborn, MA 01770
Telephone (508) 651-1120

PLACE OF BIRTH: Dearborn, MI

EDUCATION:

1974	B.A. cum laude Chemistry, with Departmental Honors Oakland University, Rochester, MI 48063
1982	Ph.D. (Pharmacology) Northwestern University, Evanston, IL 60201
1982	M.D. Northwestern University, Chicago, IL 60611

POSTDOCTORAL TRAINING:

INTERNSHIPS AND RESIDENCIES:

1983	Transitional Resident Carney Hospital, Boston, MA 02124
1984-1986	Resident in Anesthesia Massachusetts General Hospital, Boston, MA 02114

RESEARCH FELLOWSHIPS:

1986-1988	Department of Anesthesia Massachusetts General Hospital, Boston, MA 02114

LICENSURE AND CERTIFICATION:

1984	Massachusetts
1987	American Board of Anesthesiology
1990	Maine
2005	American Board of Anesthesiology, Maintenance of Certification in Anesthesiology

ACADEMIC APPOINTMENTS:

1977-1979	Lecturer in Pharmacology, Illinois College of Podiatric Medicine
1979-1982	Lecturer in Pharmacology, Illinois College of Optometry
1984-1987	Clinical Fellow in Anæsthesia, Harvard Medical School
1987-1990	Instructor in Anæsthesia, Harvard Medical School
1990-1997	Assistant Professor of Anæsthesia, Harvard Medical School
1997-2000	Associate Professor of Anæsthesia, Harvard Medical School
2000-	Professor and Academic Vice Chair of Anesthesiology Professor of Biochemistry & Molecular Pharmacology University of Massachusetts Medical School

HOSPITAL APPOINTMENTS:

1986-1990	Assistant in Anesthesia, Massachusetts General Hospital
1990-1996	Assistant Anesthetist, Massachusetts General Hospital
1996-2000	Associate Anesthetist, Massachusetts General Hospital
2000-2002	Clinical Associate in Anesthesia, Massachusetts General Hospital
2000-	Anesthesiologist, UMass Memorial Medical Center

AWARDS AND HONORS:

1972	Michigan Higher Education Association Scholarship
1972-1974	Oakland University Competitive Scholarship
1973-1974	National Merit Scholarship
1979	American Society for Pharmacology and Experimental Therapeutics Travel Award
1981	Biophysical Society Samuel A. Talbot Award
1982	Alpha Omega Alpha Research Award
1986-1988	NIH National Research Service Award
2001	Distinguished Alumnus Award Oakland University Department of Chemistry
2002	Outstanding Teacher Award University of Massachusetts Department of Anesthesiology
2003	Outstanding Medical Educator Award University of Massachusetts Medical School
2003	Outstanding Teacher Award University of Massachusetts Department of Anesthesiology
2004-	Listed in **Who's Who in America**
2005	Teaching Recognition Award, Honorable Mention International Anesthesia Research Society

MEMBERSHIPS IN PROFESSIONAL SOCIETIES:

Association of University Anesthesiologists
American Society of Anesthesiologists
American Society for Pharmacology and Experimental Therapeutics
American Society for Clinical Pharmacology and Therapeutics
International Anesthesia Research Society
Biophysical Society
International Society for Anesthetic Pharmacology
Massachusetts Medical Society
Anesthesia History Association

RESEARCH INTERESTS:

Intravenous anesthetics
Antiemetics
Monitoring depth of anesthesia
Malignant hyperthermia

RESEARCH FUNDING:

1986-1988	National Institutes of Health GM11656 (PI) The role of glutathione in malignant hyperthermia
1988-1989	Anaquest, Inc. (PI) Comparison of the sedative effects of midazolam and butorphanol
1989-1990	Glaxo, Inc. (Co-I) A randomized, double-blind comparison of intravenous ondansetron and placebo in the prevention of postoperative nausea and vomiting in female patients undergoing abdominal gynecological surgical procedures
1990-1991	Glaxo, Inc. (Co-I) A randomized, double-blind, placebo-controlled study of the effects of two dose levels of intravenous ondansetron on respiratory depression induced by alfentanil in healthy male volunteers
1991-1992	Glaxo, Inc. (Co-I) A dose finding and comparative trial of GI87084B and alfentanil for anesthesia maintenance
1992-1993	Glaxo, Inc. (Co-I) Pharmacokinetics and pharmacodynamics of GI87084B in subjects with hepatic impairment compared to subjects with normal hepatic function

1993-1994	Marion Merrell Dow, Inc. (PI) A randomized, double-blind, placebo-controlled, dose response trial to assess single dose intravenous dolasetron mesylate in patients experiencing postoperative nausea and vomiting
1993-1994	Marion Merrell Dow, Inc. (PI) A randomized, double-blind, placebo-controlled, dose response trial to assess single dose intravenous dolasetron mesylate in preventing postoperative nausea and vomiting
1993-1994	Glaxo, Inc. (Co-I) Pharmacokinetics and pharmacodynamics of GI87084B in subjects with renal impairment compared to subjects with normal renal function
1995-1996	Glaxo, Inc. (PI) A randomized, double-blind, dose-response study of ondansetron in the prevention of postoperative nausea and vomiting in inpatients
1996-1997	Aradigm Corporation (Co-I) Comparison of the pharmacokinetics and pharmacodynamics of inhaled versus intravenous morphine sulfate in healthy volunteers
1999-2000	Searle, Inc. (PI) Clinical Protocol for a Double-blind, Placebo-Controlled, Randomized Study of the Efficacy of Parecoxib 20 mg IV and Parecoxib 40 mg IV Given Postoperatively to Determine Narcotic-Sparing Effectiveness in a Post-General Surgery Pain Model

CLINICAL RESPONSIBILITIES:

1986-1988	Attending Anesthesiologist (20% clinical responsibility) Massachusetts General Hospital
1988-2000	Attending Anesthesiologist (50% clinical responsibility) Massachusetts General Hospital
1994-1997	Team Leader, East-West Anesthesia Service Massachusetts General Hospital
1997-2000	Team Leader, General Surgery Anesthesia Service Massachusetts General Hospital
2000-	Attending Anesthesiologist (45% clinical responsibility) UMass Memorial Medical Center

TEACHING EXPERIENCE:

1976-1980	Dental Hygiene Pharmacology Northwestern University Dental School 5 hours and Course Director
1977-1979	Medical Pharmacology Illinois College of Podiatric Medicine 22 hours and Course Director
1978-1981	Dental Pharmacology Northwestern University Dental School 3 hours
1979-1982	General Pharmacology Illinois College of Optometry 20 hours and Course Director
1979-1982	Ocular Pharmacology Illinois College of Optometry 10 hours and Course Director
1980-1981	Nursing Pharmacology, Northwestern University 5 hours
1994-	HST 150 Introduction to Pharmacology Harvard-MIT Program in Health, Science and Technology 4 hours
1996-	Harvard Anesthesia Review and Update 1-2 hrs
2001-	Medical Pharmacology University of Massachusetts Medical School 11-16 hrs and Course Co-Director
2007-	Medical Biochemistry University of Massachusetts Medical School 2 hrs

VISITING PROFESSORSHIPS:

April 6-7, 1994:	University of Pennsylvania
May 17-18, 1994:	University of North Carolina at Chapel Hill
Sept. 20-22, 1994:	State University of New York at Stony Brook
April 5-6, 1995:	Albany Medical College
May 8-10, 1997:	University of Texas Southwestern Medical Center
Dec. 8-9, 1998	Temple University
Dec. 16-17, 1998	University of Pittsburgh

COMMITTEE MEMBERSHIPS:

LOCAL:

2000 -	Pharmacy and Therapeutics Committee UMass Memorial Medical Center
2001 -	Physician Health and Well-Being Committee UMass Memorial Medical Center
2001 -	Educational Policy Committee University of Massachusetts Medical School
2008 -	Ethics Committee University of Massachusetts Medical School

NATIONAL:

1999 -2002	Subcommittee on Anesthetic Action and Biochemistry American Society of Anesthesiologists
2001 -	Subcommittee on Drug Disposition American Society of Anesthesiologists

EDITORIAL BOARD MEMBERSHIPS:

2000 -	International Anesthesiology Clinics
2008 -	AccessAnesthesiology (Editor-in-Chief)

BIBLIOGRAPHY:

ORIGINAL REPORTS:

1. Novak RF, Dershwitz M, Novak FC. The interaction of benzene with human hemoglobin as studied by ^1H Fourier transform NMR spectroscopy. **Biochem. Biophys. Res. Commun.** 1978; 82:634-40.

2. Novak RF, Dershwitz M, Novak FC. Characterization of the interaction of the aromatic hydrocarbons benzene and toluene with human hemoglobin. **Mol. Pharmacol.** 1979; 16:1046-58.

3. Dershwitz M, Novak RF. Lack of inhibition of glutathione reductase by unnitrated derivatives of nitrofurantoin. **Biochem. Biophys. Res. Commun.** 1980; 92:1313-19.

4. Dershwitz M, Novak RF. Lack of inhibition of glutathione reductase by anthracycline antibiotics. **Biochem. Pharmacol.** 1981; 30:676-8.

5. Dershwitz M, Novak RF. Generation of superoxide anion via the interaction of nitrofurantoin with human hemoglobin. **J. Biol. Chem.** 1982; 257:75-9.

6. Dershwitz M, Novak RF. Studies on the mechanism of nitrofurantoin-mediated red cell toxicity. **J. Pharm. Exp. Ther.** 1982; 222:430-4.

7. Dershwitz M, Ts'ao CH, Novak RF. Metabolic and morphologic effects of the antimicrobial agent nitrofurantoin on human erythrocytes in vitro. **Biochem. Pharmacol.** 1985; 34:1963-70.

8. Dershwitz M, Sréter FA, Ryan JF. Ketamine does not trigger malignant hyperthermia in susceptible swine. **Anesth. Analg.** 1989; 69:501-3.

9. Dershwitz M, Ryan JF, Guralnick W. Safety of amide local anesthetics in patients susceptible to malignant hyperthermia. **J. Am. Dent. Assoc.** 1989; 118:276-80.

10. Dershwitz M, Sréter FA. Azumolene reverses episodes of malignant hyperthermia in susceptible swine. **Anesth. Analg.** 1990; 70:253-5.

11. Dershwitz M, Rosow CE, Di Biase PM, Zaslavsky A. Comparison of the sedative effects of butorphanol and midazolam. **Anesthesiology** 1991; 74:717-24.

12. Dershwitz M, Sherman EP. Acute myocardial infarction symptoms masked by epidural morphine? **J. Clin. Anesth.** 1991; 3:146-8.

13. Dershwitz M, Rosow CE, Di Biase PM, Joslyn AF, Sanderson PE. Ondansetron is effective in decreasing postoperative nausea and vomiting. **Clin. Pharmacol. Ther.** 1992; 52:96-101.

14. Dershwitz M, Di Biase PM, Rosow CE, Wilson RS, Sanderson PE, Joslyn AF. Ondansetron does not affect alfentanil-induced ventilatory depression or sedation. **Anesthesiology** 1992; 77:447-52.

15. McKenzie R, Sharifi-Azad S, Dershwitz M, Miguel R, Joslyn A, Tantisira B, Rosenblum F, Rosow C, Downs J, Bowie J, Odell S, Lessin J, Di Biase P, Nations M. A randomized, double-blind pilot study examining the use of intravenous ondansetron in the prevention of postoperative nausea and vomiting in female inpatients. **J. Clin. Anesth.** 1993; 5:30-6.

16. Dershwitz M, Randel GI, Rosow CE, Fragen RJ, Connors PM, Librojo ES, Shaw DL, Peng AW, Jamerson BD. Initial clinical experience with remifentanil, a new opioid metabolized by esterases. **Anesth. Analg.** 1995; 81:619-23.

17. Dershwitz M, Hoke JF, Rosow CE, Michałowski P, Connors PM, Muir KT, Dienstag JL. Pharmacokinetics and pharmacodynamics of remifentanil in volunteer subjects with severe liver disease. **Anesthesiology** 1996; 84:812-20.

18. Dershwitz M, Rosow CE. The pharmacokinetics and pharmacodynamics of remifentanil in volunteers with severe hepatic or renal dysfunction. **J. Clin. Anesth.** 1996; 8:88S-90S.

19. Kovac AL, Scuderi PE, Boerner TF, Chelly JE, Goldberg ME, Hantler CB, Hahne WF, Brown RA, Dolasetron Mesylate PONV Treatment Study group. Treatment of postoperative nausea and vomiting with single intravenous doses of dolasetron mesylate: a multicenter trial. **Anesth Analg** 1997; 85:546-52.

20. Hoke JF, Shlugman D, Dershwitz M, Michałowski P, Malthouse-Dufore S, Connors PM, Marten D, Rosow CE, Muir KT, Rubin N, Glass PSA. Pharmacokinetics and pharmacodynamics of remifentanil in subjects with renal failure compared to healthy volunteers. **Anesthesiology** 1997; 87:533-41.

21. Gan TJ, Glass PS, Windsor A, Payne F, Rosow C, Sebel P, Manberg P, BIS Utility Study Group. Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. **Anesthesiology** 1997; 87:808-15.

22. Kearse LA, Rosow C, Zaslavsky A, Connors P, Dershwitz M, Denman W. Bispectral analysis of the electroencephalogram predicts conscious processing of information during propofol sedation and hypnosis. **Anesthesiology** 1998; 88:25-34.

23. Dershwitz M, Conant JA, Chang YC, Rosow CE, Connors PM. A randomized double-blind dose-response study of ondansetron in the prevention of postoperative nausea and vomiting. **J Clin Anesth** 1998; 10:314-20.

24. Philip BK, Pearman MH, Kovac AL, Chelly JE, Wetchler BV, McKenzie R, Monk TG, Dershwitz M, Mingus M, Sung YF, Hahne WF, Brown RA, Dolasetron PONV Prevention Study Group. Dolasetron for the prevention of postoperative nausea and vomiting following outpatient surgery with general anaesthesia: a randomized, placebo-controlled study. **Eur J Anaesthesiol** 2000; 17:23-32.

25. Philip BK, McLeskey CH, Chelly JE, McKenzie R, Kovac AL, Diemunsch P, DuBois DM, Dolasetron Prophylaxis Study Group. Pooled analysis of three large clinical trials to determine the optimal dose of dolasetron mesylate needed to prevent postoperative nausea and vomiting. **J Clin Anesth** 2000; 12:1-8. (erratum published in **J Clin Anesth** 2000; 12:577-78).

26. Dershwitz M, Walsh JL, Morishige RJ, Connors PM, Rubsamen RM, Shafer, SL, Rosow C. Pharmacokinetics and pharmacodynamics of inhaled versus intravenous morphine in healthy volunteers. **Anesthesiology** 2000; 93:619-28.

27. Dershwitz M, Michałowski P, Chang YC, Rosow CE, Conlay LA. Postoperative nausea and vomiting following total intravenous anesthesia with propofol and remifentanil or alfentanil. How important is the opioid? **J Clin Anesth** 2002; 14:275-78.

28. Dershwitz M. Droperidol: should the black box be light gray? **J Clin Anesth** 2002; 14:598-603.

29. Dershwitz M. There should be a threshold dose for the FDA black-box warning on droperidol (letter). **Anesth Analg** 2003; 97:1542-3.

30. Dershwitz M. Is droperidol safe? Probably... **Semin Anesth** 2004; 23:291-301.

31. Cooper JB, Blum RH, Carroll JS, Dershwitz M, Feinstein DM, Gaba DM, Morey JC, Singla AK. Differences in safety climate among hospital anesthesia departments and the effect of a realistic simulation-based training program. **Anesth Analg** 2008; 106: 574-584.

PROCEEDINGS OF MEETINGS:

1. Kharasch ED, Dershwitz M, Novak RF. Differential hemeprotein involvement in microsomal and red cell lysate quinone and nitro group reduction. In: Sato R, Kato R, eds. **Microsomes, Drug Oxidations, and Drug Toxicity**. New York: Wiley Interscience, 1982:237-8.

BOOKS:

1. Stelmack TR, Dershwitz M. **Manual for the Use of Pharmaceutical Agents for Ocular Diagnostic Purposes,** ICO Press, Chicago, 1980.

2. Dershwitz M, ed. **The MGH Board Review of Anesthesiology.** 4th ed. Norwalk, CT: Appleton & Lange, 1994.

3. Dershwitz M, ed. **The MGH Board Review of Anesthesiology.** 5th ed. Norwalk, CT: Appleton & Lange, 1998.

4. Dershwitz M, Walz JM, eds. **McGraw-Hill Specialty Board Review: Anesthesiology.** 6th ed. New York: McGraw-Hill, 2006.

CHAPTERS IN BOOKS:

1. Dershwitz M, Ten Eick RE. Pharmacology. In: **National Boards Examination Review for Part I, Basic Sciences.** Garden City, NY: Medical Examination Publishing Co., 1981.

2. Dershwitz M. Pharmacology. In: **National Boards Examination Review for Part I, Basic Sciences.** New Hyde Park, NY: Medical Examination Publishing Co., 1984.

3. Dershwitz M. Pharmacology. In: **National Boards Examination Review for Part I, Basic Sciences.** New York: Elsevier Science Publishing Co., Inc., 1987.

4. Dershwitz M. Local anesthetics. In: Firestone LL, Lebowitz PW, Cook CE, eds. **Clinical Anesthesia Procedures of the Massachusetts General Hospital,** 3rd ed. Boston: Little, Brown and Co., 1988.

5. Dershwitz M. Antiemetics. In: Bowdle TA, Horita A, Kharasch ED, eds. **The Pharmacological Basis of Anesthesia.** New York: Churchill Livingstone, 1994.

6. Dershwitz M. Antiemetic drugs. In: White PF, ed. **Ambulatory Anesthesia and Surgery.** London: W.B. Saunders Co., 1997.

7. Rosow CE, Dershwitz M. Opioid analgetics. In: Longnecker DE, Tinker JH, Morgan GE, eds. **Principles and Practice of Anesthesiology,** 2nd ed. Philadelphia: Mosby-Year Book, Inc., 1997.

8. Stambach A, Dershwitz M. Intravenous and inhalation anesthetics. In: Hurford WE, Bailin MT, Davison JK, et al., eds. **Clinical Anesthesia Procedures of the Massachusetts General Hospital,** 5th ed. Philadelphia: Lippincott-Raven, 1998.

9. Dershwitz M. Agents for general anesthesia. In: Schirmer BD, Rattner DW, eds. **Ambulatory Surgery.** Philadelphia: W.B. Saunders Co., 1998.

10. Dershwitz M. Intravenous and inhalation anesthetics. In: Hurford WE, ed. **Clinical Anesthesia Procedures of the Massachusetts General Hospital**, 6th ed. Philadelphia: Lippincott Williams and Wilkins, 2002.

11. Dershwitz M, Landow L, Joshi-Ryzewicz W. Anesthesia for bedside procedures. In: Irwin RS, Cerra FB, Rippe JM, eds. **Irwin and Rippe's Intensive Care Medicine**, 5th ed. Philadelphia: Lippincott, Williams, and Wilkins, 2003.

12. Dershwitz M, Landow L, Joshi-Ryzewicz W. Anesthesia for bedside procedures. In: Irwin RS, Rippe JM, Curley FJ, Heard SO, eds. **Procedures and Techniques in Intensive Care Medicine**, 3rd ed. Philadelphia: Lippincott, Williams, and Wilkins, 2003.

13. Dershwitz M. Antipsychotics. In: Fink M, Abraham E, Vincent J-L, et al., eds. **Textbook of Critical Care**, 5th ed. Philadelphia: Elsevier, 2005.

14. Dershwitz M. Analgesic cyclooxygenase inhibitors for ambulatory anesthesia. In: Steele S, Nielsen K, eds. **Ambulatory Anesthesia and Perioperative Analgesia**. New York: McGraw Hill, 2005.

15. Walz JM, Dershwitz M. Anesthesia for bedside procedures. In: Irwin RS, Rippe JM, eds. **Manual of Intensive Care Medicine**, 4th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.

16. Dershwitz M. Anesthesia for bedside procedures. In: Irwin RS, Rippe JM, eds. **Irwin and Rippe's Intensive Care Medicine**, 6th ed. Philadelphia: Lippincott, Williams, and Wilkins, 2007.

17. Dershwitz M. Anesthesia for bedside procedures. In: Irwin RS, Rippe JM, Lisbon A, Heard SO, eds. Procedures, Techniques, and Minimally Invasive Monitoring in Intensive Care Medicine, 4th ed. Philadelphia: Lippincott, Williams, and Wilkins, 2007.

18. Dershwitz M, Rosow CE. Intravenous anesthetics. In: Longnecker DE, Brown D, Newman M, Zapol WM, eds. **Anesthesiology**, 3rd ed. New York: McGraw-Hill, 2008.

19. Rosow CE, Dershwitz M. Opioid analgesics. In: Longnecker DE, Brown D, Newman M, Zapol WM, eds. **Anesthesiology**, 3rd ed. New York: McGraw-Hill, 2008.

20. Dershwitz M, Rosow CE. Appendix A: Formulary. In: Longnecker DE, Brown D, Newman M, Zapol WM, eds. **Anesthesiology**, 3rd ed. New York: McGraw-Hill, 2008.

REVIEWS AND EDUCATIONAL MATERIALS:

1. Dershwitz M. Advances in antiemetic therapy. **Anesth. Clinics North Amer.** 1994; 12:119-32.

2. Dershwitz M. How can the costs of anesthesia be decreased? **Intravenous Anesth. Today** 1994; 1(3):4-9.

3. Dershwitz M. 5-HT_3 antagonists in postoperative nausea and vomiting. **Ambulatory Anesth.** 1995; 10(1):9-11.

4. Ballantyne JC, Dershwitz M. The pharmacology of non-steroidal anti-inflammatory drugs for acute pain. **Curr. Opin. Anaesthesiol.** 1995; 8:461-68.

5. Dershwitz M, Rosow CE. Remifentanil: a truly-short-acting opioid. **Semin. Anesth.** 1996; 15:88-96.

6. Dershwitz M, Rosow CE. Remifentanil: an opioid metabolized by esterases. **Exp Opin Invest Drugs** 1996; 5:1361-76.

7. Dershwitz M. Should we measure depth of anesthesia? **Semin. Anesth.** 2001; 20:246-56.

8. Dershwitz M, Henthorn TK. The pharmacokinetics and pharmacodynamics of thiopental as used in lethal injection. **Fordham Urban Law J** 2008; 35:931-56.

NON-PRINT MATERIALS:

1. Dershwitz M. Use of short-acting analgesia in surgery: achieving cost-effective care (videotape). Rancho Mirage, CA: Annenberg Center for Health Sciences, 1996.

2. Dershwitz M. General considerations (section editor). In: Bailin M. ed. **Harvard Department of Anesthesia Electronic Library** (CD-ROM). Philadelphia: Lippincott Williams & Wilkins, 2001.

3. Dershwitz M. Practical pharmacokinetics of intravenous anesthetics. In: Bailin M. ed. **Harvard Department of Anesthesia Electronic Library** (CD-ROM). Philadelphia: Lippincott Williams & Wilkins, 2001.

ABSTRACTS:

1. Bruer P, Cantarella J, Dershwitz M, Undy L, Young DC. Polarographic studies of copper (II) complexes of glycine peptides. Abstract #6, Anachem Society Meeting, Detroit, MI, 1976.

2. Dershwitz M, Novak RF. The interaction of nitrofurantoin with human hemoglobin. **Fed. Proc.** 1979; 38:544.

3. Dershwitz M, Novak RF. Metabolic effects of nitrofurantoin on the human erythrocyte. **The Pharmacologist** 1979; 21:170.

4. Dershwitz M, Novak RF. Depletion of erythrocyte adenosine-5'-triphosphate and reduced glutathione levels by nitrofurantoin and unnitrated derivatives. **Fed. Proc.** 1980; 39:748.

5. Dershwitz M, Lack of inhibition of glutathione reductase by unnitrated derivatives of nitrofurantoin. **Fed. Proc.** 1980; 39:1751.

6. Dershwitz M, Novak RF. Oxidation of human hemoglobin by nitrofurantoin. **Biophys. J.** 1981; 33:81a.

7. Dershwitz M, Novak RF. The effects of ethyl isocyanide on nitrofurantoin-mediated depletion of red cell glutathione. **Fed. Proc.** 1981; 40:667.

8. Dershwitz M, Novak RF. Studies on the mechanism of nitrofurantoin-mediated red cell toxicity. **Eighth International Congress on Pharmacology,** Tokyo, Japan, 1981.

9. Kharasch ED, Dershwitz M, Novak RF. Differential hemeprotein involvement in microsomal and red cell lysate quinone and nitro group reduction. **Fifth International Symposium on Microsomes and Drug Oxidations,** Tokyo, Japan, 1981.

10. Dershwitz M, Novak RF. On the mechanism of nitrofurantoin-mediated red cell toxicity. **The Pharmacologist** 1981; 23:211.

11. Dershwitz M, Novak RF. Generation of activated oxygen species in human red cells by nitrofurantoin. **Seventh International Biophysics Congress and Third Pan-American Biochemistry Congress,** Mexico City, Mexico, 1981.

12. Dershwitz M, Sréter FA. Substrate requirements for glutathione maintenance in pig red cells in vitro. **The Pharmacologist** 1987; 29:210.

13. López JR, Dershwitz M, Sanchez V, Sréter FA. $[K^+]$ and $[Na^+]$ in malignant hyperthermia-susceptible swine. **Biophys. J.** 1988; 53:609a.

14. Chang RJ, Dershwitz M, Sréter FA, Smilowitz H. Skeletal muscle from malignant hyperthermia-susceptible swine contains decreased levels of monoclonal antibody reactive dihydropyridine receptor. **The Pharmacologist** 1988; 30:A88.

15. Kim DH, Lee YS, Sréter FA, Ohkisa T, Dershwitz M, Ikemoto N. Effects of azumolene on the kinetics of Ca release from normal and malignant hyperthermic sarcoplasmic reticulum. **Biophys. J.** 1990; 57:497a.

16. Dershwitz M, Sréter FA. Reversal of malignant hyperthermia episodes by azumolene in susceptible swine. **Anesth. Analg.** 1990; 70:S81.

17. Dershwitz M, Rosow CE, Di Biase PM, Zaslavsky A. Characterization of the sedative effects of butorphanol in humans. **The Pharmacologist** 1990; 32:139.

18. Dershwitz M, Rosow CE, Di Biase PM, Joslyn AF, Sanderson PE. Prophylaxis of postoperative vomiting by ondansetron. **Clin. Pharm. Ther.** 1991; 49:184.

19. Dershwitz M, Rosow CE, Di Biase PM, Joslyn AF, Sanderson PE. Ondansetron is effective in decreasing postoperative nausea and vomiting. **Jap. J. Anesthesiol.** 1991; 40:S312.

20. Dershwitz M, Di Biase PM, Rosow CE, Wilson RS. Ondansetron does not affect alfentanil-induced ventilatory depression. **Anesthesiology** 1991; 75:A321.

21. Nakamura H, deBros F, Roberts J, Dershwitz M, Sweet W, Poletti C, Philbin D. Plasma catecholamine concentrations before and after trigeminal rhizotomy: a clinical study. 5th International Symposium on Endocrinology in Anesthesia and Critical Care, Berlin, October, 1991.

22. Nakamura H, deBros F, Roberts J, Dershwitz M, Sweet W, Poletti C, Philbin D. Plasma catecholamine concentrations before and after trigeminal rhizotomy: a clinical study. **Anesth. Analg.** 1992; 74:S217.

23. Dershwitz M, Randel G, Rosow CE, Fragen R, Di Biase PM, Librojo ES, Jamerson B, Shaw DL. Dose-response relationship of GI87084B, a new ultra-short acting opioid. **Anesthesiology** 1992; 77:A396.

24. Dershwitz M, Rosow CE, Di Biase PM, Wilson RS. Ventilatory depression during and after a low dose alfentanil infusion in normal volunteers. **Anesthesiology** 1992; 77:A360.

25. Dershwitz M, Rosow CE, Michałowski P, Connors PM, Hoke JF, Muir KT, Dienstag JL. Pharmacokinetics and pharmacodynamics of remifentanil in volunteer subjects with severe liver disease. Association of University Anesthesiologists Annual Meeting; Chicago, Illinois; May, 1994.

26. Dershwitz M, Rosow CE, Michałowski P, Connors PM, Hoke JF, Muir KT, Dienstag JL. Pharmacokinetics and pharmacodynamics of remifentanil in subjects with severe liver disease compared with normal subjects. **Anesthesiology** 1994; 81:A377.

27. Shlugman D, Dufore S, Dershwitz M, Michałowski P, Hoke J, Muir KT, Rosow C, Glass PSA. Respiratory effects of remifentanil in subjects with severe renal impairment compared to matched controls. **Anesthesiology** 1994; 81:A1417.

28. Hoke JF, Muir KT, Glass PSA, Shlugman D, Rosow CE, Dershwitz M, Michałowski P. Pharmacokinetics of remifentanil and its metabolite (GR90291) in subjects with renal disease. **Clin. Pharm. Ther.** 1995; 57:148.

29. Kovac A, Melson T, Graczyk S, Scuderi P, Watkins WD, MCPR44 Study Group. Treatment of postoperative nausea and vomiting with single doses of IV dolasetron: a multicenter trial. **Anesthesiology** 1995; 83:A6.

30. Kearse L, Rosow C, Connors P, Denman W, Dershwitz M. Propofol sedation/hypnosis and bispectral EEG analysis in volunteers. **Anesthesiology** 1995; 83:A506.

31. Kovac A, Chelly J, McKenzie R, Philip B, Pearman M, Brown R, MCPR45 Study Group. Multicenter intravenous dose response trial to assess the efficacy and safety of dolasetron mesylate in preventing postoperative nausea and vomiting. **Anesthesiology** 1996; 85:A1.

32. Dershwitz M, Conant JA, Rosow CE, Connors PM, Zaslavsky A. A dose-response study of ondansetron in preventing postoperative nausea and vomiting in female inpatients. **Anesthesiology** 1996; 85:A331.

33. Rosow CE, Connors PM, Hennessy D, Rosow D, Dershwitz M, Shyu WC, Vachharajani N. Bioavailability of nasal butorphanol. **Anesthesiology** 1996; 85:A314.

34. Denman WT, Rosow D, Hennessy D, Dershwitz M, Rosow C. Miotic effects of alfentanil, and fentanyl occur at extremely low doses. **The Pharmacologist** 1997; 39:109.

35. Dershwitz M, Morishige RJ, Walsh JL, Rodriguez-Paz JM, Maarschalk LA, Rubsamen RM, Connors PM, Rosow CE. Pharmacokinetics of inhaled morphine in normal volunteers. **Anesthesiology** 1997; 87:A376.

36. Denman WT, Rosow D, Hennessy D, Dershwitz M, Rosow CE. Miotic effects of alfentanil, and fentanyl occur at extremely low doses. **Anesthesiology** 1997; 87:A316.

37. Michałowski P, Dershwitz M, Rosow CE, Conlay LA, Chang YC. Total intravenous anesthesia with remifentanil or alfentanil in ambulatory orthopedic surgery carries minimal risk of postoperative nausea and vomiting. **Anesthesiology** 1998; 89:A34.

38. Walsh J, Dershwitz M, Rosow C, Connors PM, Morishige R, Rubsamen R. Intravenous and inhaled morphine pharmacokinetics and pharmacodynamics as measured by pupillometry. **Anesthesiology** 1998; 89:A521.

39. Dershwitz M, Walsh JL, Krause S, Makris N, Gollub R. Using functional magnetic resonance imaging to measure opioid effects in discrete brain regions. Association of University Anesthesiologists Annual Meeting; Pittsburgh, Pennsylvania; May, 1999.

40. Gollub RL, Breiter H, Dershwitz M, Elman I, Kantor H, Gastfriend D, Benson E, Lazar S, Krause S, Makris N, Kennedy D, Campbell T, Weisskoff R, Rosen B: Cocaine dose dependent activation of brain reward circuitry in humans revealed by 3T fMRI. International Conference on Functional Mapping of the Human Brain, 1999.

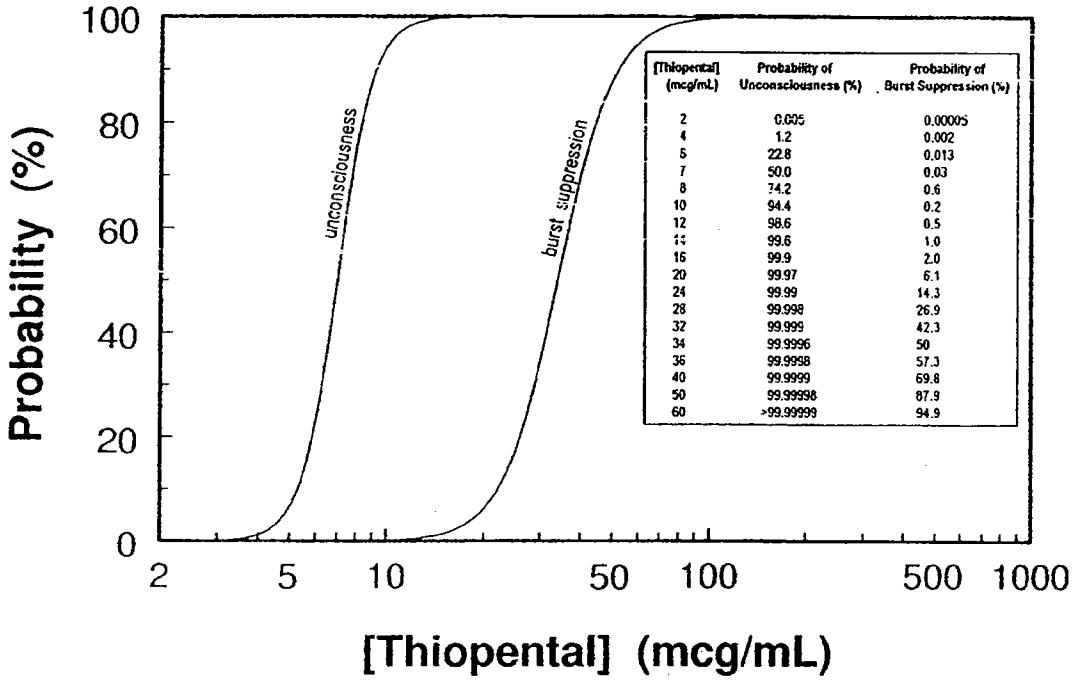
41. Dershwitz M, Walsh JL, Krause S, Makris N, Gollub R. Using functional magnetic resonance imaging to measure opioid effects in discrete brain regions. **Anesthesiology** 1999; 91:A367.

42. He YL, Walsh J, Denman W, Dershwitz M, Kim J, Rosow C. Pharmacodynamic modeling of the miotic effects of alfentanil in humans measured with infrared pupillometry. Association of University Anesthesiologists Annual Meeting; Rochester, NY; May, 2001.

43. Gollub R, Aquino P, Kong J, Gracely R, Kramet T, Dershwitz M. Reliable intensity and laterality encoding of noxious pressure and heat pain in cortex within single subjects using 1.5T fMRI. Organization for Human Brain Mapping 7th Annual Meeting; Brighton, UK; June, 2001.

44. Aquino P, Kong J, Gracely RH, Kramer T, Dershwitz M, Gollub R. Reliable encoding of brief noxious mechanical stimuli in single subjects using 1.5T fMRI. Society for Neuroscience, 2001.

EXHIBIT B



[Thiopental] (mcg/mL)	Probability of Unconsciousness (%)	Probability of Burst Suppression (%)
2	0.005	0.00005
4	1.2	0.002
5	22.8	0.013
7	50.0	0.03
8	74.2	0.6
10	94.4	0.2
12	98.6	0.5
14	99.6	1.0
16	99.9	2.0
20	99.97	6.1
24	99.99	14.3
28	99.998	26.9
32	99.999	42.3
34	99.9996	50
36	99.9998	57.3
40	99.9999	69.8
50	99.99998	87.9
60	>99.99999	94.9

EXHIBIT C

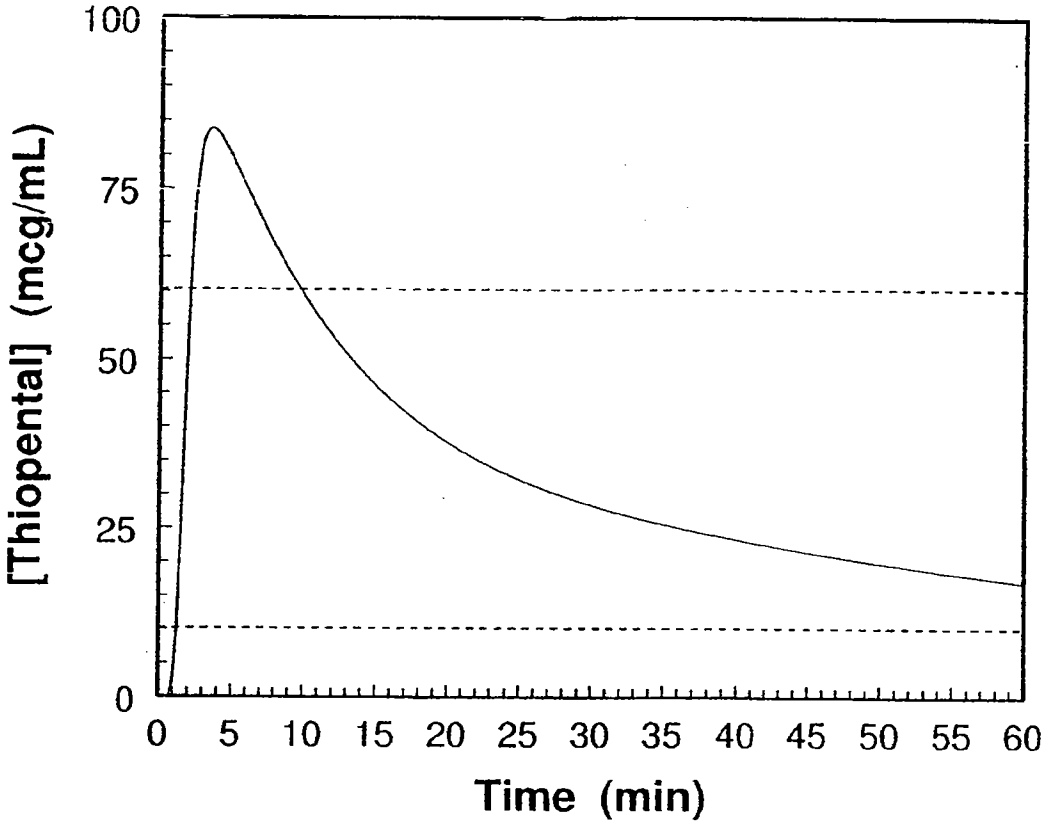

100
75
50
25
0
[Thiopental] (mcg/mL)
0 5 10 15 20 25 30 35 40 45 50 55 60
Time (min)

Exhibit D

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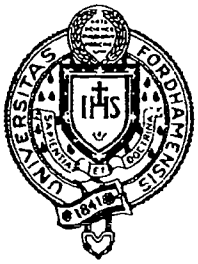

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THE PHARMACOKINETICS AND PHARMACODYNAMICS OF THIOPENTAL AS USED IN LETHAL INJECTION

Mark Dershwitz, M.D., Ph.D. & Thomas K. Henthorn, M.D.***

Thiopental (sometimes called, although inaccurately, Sodium Pentothal) was the most commonly used intravenous anesthetic agent for about fifty years, beginning in the mid-1940s.[1] As states began to discuss and develop protocols for lethal injection in the 1970s, thiopental was the logical choice as the medication to render the inmate unconscious prior to the administration of subsequent medications, most commonly pancuronium (a medication that paralyzes skeletal muscle and results in cessation of breathing) followed by potassium chloride (a salt that is a necessary component of the diet but when given intravenously in large doses results in the cessation of electrical activity in the heart).

It is virtually unanimously accepted by physicians, particularly anesthesiologists, that the administration of lethal doses of pancuronium and/or potassium chloride to a conscious person would result in extreme suffering. For this reason, all of the protocols for lethal injection that we have reviewed precede the administration of pancuronium and potassium chloride with a dose of thiopental intended to render the inmate unconscious for a period of time far in excess of that necessary to complete the execution.[2] When implemented as written, meaning the correct doses of the correct medications are administered in the correct order into a properly functioning intravenous delivery system and with sufficient time for thiopental to produce its effect, all of the protocols we have reviewed are intended to result in the rapid death of the inmate without undue pain or suffering.

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1. *See* A.S. Evers et al., *General Anesthetics*, *in* GOODMAN & GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS 341, 342 (Laurence L. Brunton et al. eds., McGraw-Hill, 11th ed. 2006).

2. One or both of the authors has reviewed the protocols used by Alabama, Arkansas, California, Delaware, Florida, Georgia, Kentucky, Maryland, Missouri, Montana, North Carolina, Ohio, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and the federal government.

This paper will concentrate on the pharmacokinetics and pharmacodynamics of thiopental. As applied here, pharmacokinetics is the study of the concentration of thiopental as a function of time in tissues (particularly brain), while pharmacodynamics is the study of the effects of thiopental (particularly the production of unconsciousness and impairment of the heart's ability to circulate blood).[3] By using generally accepted computer modeling techniques, and considering the wealth of published studies on the pharmacology of thiopental, we can prepare predictions of such relevant parameters as the onset (how long it takes for the inmate to become unconscious) and duration (how long the inmate would remain unconscious) of the pharmacological effects of thiopental.[4]

Thiopental is usually described as an "ultra-short acting" sedative/hypnotic agent in pharmacology and anesthesiology texts.[5] This description is semantically correct, but only when thiopental is compared to other barbiturates. Indeed, when thiopental was used to induce (i.e., begin) a general anesthetic, the typical adult dose was about 300 mg and the typical patient would remain unconscious for 5 to 10 minutes.[6] The usual anesthetic regimen would involve the subsequent administration of anesthetic gases that would keep the patient unconscious for the duration of the surgical procedure. The protocols for lethal injection mandate doses of thiopental ranging from 2000 to 5000 mg, i.e., about seven to sixteen times higher than those used to begin a typical anesthetic.[7] However, the relationship between the dose of thiopental and its duration of action is *not* linear. For example, as the dose of thio-

3. K.B. Johnson & Talmage D. Egan, *Principles of Pharmacokinetics and Pharmacodynamics: Applied Clinical Pharmacology for the Practitioner*, *in* ANESTHESIOLOGY 821, 821 (D.E. Longnecker et al. eds., McGraw-Hill 3d ed. 2008).

4. *See generally* Colin A. Shanks et al., *A Pharmacokinetic-Pharmacodynamic Model for Quantal Responses with Thiopental*, 21 J. PHARMACOKINETICS & BIOPHARMACODYNAMICS 309, 309-21 (1993) (providing the pharmacokinetic model for thiopental and the pharmacodynamic model for burst suppression); *see also* Robert J. Telford et al., *Fentanyl does not Alter the "Sleep" Plasma Concentration of Thiopental*, 75 ANESTHESIA & ANALGESIA 523, 523-29 (1993) (providing the pharmacodynamic model for unconsciousness).

5. Thiopental is "ultra-short acting" only in comparison to the barbiturates that are classified as "short-acting," "intermediate-acting," and "long-acting." This differentiation is primarily of historical interest. *See, e.g.*, LOUIS S. GOODMAN & ALFRED GILMAN, THE PHARMACOLOGICAL BASIS OF THERAPEUTICS 138 (Macmillan Co., 2d ed. 1955).

6. Mark Dershwitz & C.E. Rosow, *Intravenous Anesthetics*, *in* ANESTHESIOLOGY, *supra* note 3, at 849, 856. R

7. *See supra* note 2 for the list of states whose protocols the authors have reviewed. R

pental is increased sevenfold to 2000 mg, the duration of unconsciousness is *not* also increased sevenfold but actually much more, as described later. The pharmacological term "sedative/hypnotic" means that at low doses (e.g. 25 - 100 mg), thiopental causes sedation (i.e., sleepiness), while at higher doses it produces hypnosis (i.e., unconsciousness).[8] At sedative doses, it produces no analgesia (pain relief) and in fact probably increases the perception of painful stimuli. When a person is rendered unconscious by thiopental, the conscious perception of pain is abolished. The body may, however, react in a reflex manner to pain and exhibit such phenomena as movement, a fast heart rate, sweating, or tearing. Additionally, the state of consciousness produced by a drug is also affected by the strength of applied stimuli. Thus, at the threshold of unconsciousness pain may reverse the state and produce consciousness, making it difficult to distinguish between reflex responses to pain and conscious response. Therefore, it has been argued by some that deep unconsciousness, as defined by burst suppression on the electroencephalogram ("EEG"), be the level of unconsciousness produced in lethal injection.[9]

We will present models to describe the onset and duration of unconsciousness as a function of the dose of thiopental. For example, with the administration of 2000 mg of thiopental to an 80-kg person, loss of consciousness will occur within approximately 1.0 to 1.5 minutes, while duration of unconsciousness will last approximately two hours. The time for onset of burst suppression in the same individual would be approximately 1.5 to 2.5 minutes and would reliably last only seven minutes. Larger doses of thiopental will be shown to result in further prolongation of the duration of unconsciousness and burst suppression.

There is an enormous body of anesthesiology literature supporting the use of mathematical modeling of the pharmacokinetic and pharmacodynamic behavior of intravenous anesthetic agents like thiopental.[10] Such modeling underlies the commonly utilized tech-

8. Dershwitz & Rosow, *Intravenous Anesthetics*, *supra* note 6, at 850. R

9. *See* Testimony of Thomas K. Henthorn, Taylor vs. Crawford et al., No. 05-4173-CV-S-FJG, 2006 WL 1779035, slip op at *7 (W.D. Mo. June 26, 2006).

10. *See, e.g.*, such comprehensive review articles and book chapters as: Dershwitz & Rosow, *supra* note 6, at 849-68; J. Sear, *Total Intravenous Anesthesia*, *in* ANESTHESIOLOGY, *supra* note 3, at 897, 897-917; Thomas K. Henthorn, *The Effect of Altered Physiological States on Intravenous Anesthetics*, 182 HANDB. EXP. PHARMACOL. 363, 363-77 (2008); Thomas K. Henthorn, *Recirculatory Pharmacokinetics: Which Covariates Affect the Pharmacokinetics of Intravenous Agents?*, 523 ADV. EXP. MED. BIOL. 27, 27-33 (2003); Harmut Derendorf et al., *Pharmacokinetic/Pharmacodynamic Modeling in Drug research and Development*, 40 J. CLIN. PHARMACOL. 1399, 1399- R R R

nique of target-controlled intravenous drug infusions. Mathematical modeling of intravenous anesthetics has been extensively studied and has been validated in the real world practice of target-controlled infusions ("TCI").[11] TCI couples a small computer with an infusion pump so that multi-compartment models are used to predict and adjust anesthetic drug infusion rates on a second-by-second basis to reach and maintain plasma concentrations determined by the practitioner.[12] TCI devices are in common use in anesthetic practice worldwide. Median absolute performance errors for TCI of predicted versus actual drug concentrations are in the range of ±30% when literature values for pharmacokinetic parameters are used to drive the TCI device.[13] Therefore, similar errors can be expected when applying the simulations presented here to any given individual. Thus the methodology employed in performing the pharmacological simulations employed herein has undergone peer review and its application to the actual practice of anesthesia is well studied.

I. THE ONSET TIMES FOR THIOPENTAL ADMINISTERED AT VARIOUS RATES

No drug, including thiopental, has an effect the moment it is injected. It must first be transported by circulating blood to the site of action, i.e., the brain in the case of thiopental. The drug must then cross the blood-brain barrier to reach drug receptors in the neural cells of the brain. The drug-receptor interaction then triggers a cellular response resulting in the drug effect. As thiopental concentrations at the site of action continue to rise, more intense drug responses are seen. The interval between injecting the drug, and seeing an effect, i.e. the process of accumulating adequate drug concentrations in the blood and subsequently the brain, is called hysteresis.[14] A good way to think about hysteresis is to compare it to using a stove. Turning the flame on is akin to injecting the drug; transporting the heat to the surface of the pan is analogous to the

1418 (2000); D.R. Stanski, *Pharmacodynamic Modeling of Anesthetic EEG Drug Effects*, 32 ANNU. REV. PHARMACOL. TOXICOL. 423, 423-47 (1992).

11. *See* Talmage D. Egan, *Target-Controlled Drug Delivery: Progress Toward an Intravenous "Vaporizer" and Automated Anesthetic Administration*, 99 ANESTHESIOLOGY 1214, 1215 (2003).

12. *Id.*

13. *See id.* at 1216-17; *see also* Robert A.Veselis et al., *Performance of Computer-Assisted Continuous Infusion at Low Concentrations of Intravenous Sedatives*, 84 ANESTHESIA & ANALGESIA 1049, 1053-57 (1997).

14. Johnson & Egan, *supra* note 3, at 825. R

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circulation delivering the drug to the site of action; and cooking the food in the pan is akin to producing the drug effect. Your dinner can range from undercooked to well done, depending on how long it's exposed to the flame "dose" the stove is delivering. Similarly the heating effect continues for some time even after the flame is turned off. Therefore, with hysteresis it is possible to have the same effect at two different plasma drug concentrations just as it is possible for a pan to be at the same temperature at two different flame settings, once during heating and again during cooling. Pharmacokinetic-pharmacodynamic modeling is able to mathematically describe this hysteresis and fully explain how the same blood drug concentration can produce variable effects.[15]

In a lethal injection setting, once an injection of thiopental has begun, the drug must pass through the IV tubing from the "injection room" to the "death chamber" before reaching the vein of the condemned inmate. For instance, if the tubing is ten feet long with a typical tubing volume of 1.8 mL/foot, then the total volume is 18 mL. Assuming fluid traveling in a tube as a perfect cylinder and an injection speed of 2 mL/sec, it would take a full 9 seconds for the drug to reach the vein.

After entering the bloodstream the drug must circulate with the blood to reach the brain before concentrations at the site of effect can begin to rise. Depending on where the intravenous catheter is placed in the inmate, it could take up to 15 seconds for the drug to reach the right-sided chambers of the heart and thus be considered within the central circulation where the flow of blood is at its greatest. From the right side of the heart, the blood flows through the pulmonary arteries to the capillaries of lungs, recollects in the pulmonary veins and flows back to the left side of the heart. The powerful left ventricle of the heart then pumps the blood out through the aortic arch into all of the arteries of the body, including the carotid and vertebral arteries leading to the brain.

The principles governing the time required for an injected drug to pass through IV tubing to reach the vein also apply to the drug within the bloodstream. That is, the time elapsed is directly related to the volume of the system and the flow rate of the fluid in the system. The volume of the central circulation as a percentage of the body's total blood volume is near maximum when lying flat, approximately one third of the total blood volume or 1.7 L for the typical male inmate. It would be higher tilted head down and

15. *See generally id.* at 825.

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lower when standing. In a sedated adult it would be reasonable to assume a total blood flow (or cardiac output) of 5 L/min. Thus the time required for drug just arriving in the right side of the heart to pass through the central circulation to reach the brain would be 1.7 L divided by 5 L/min, which is approximately 20 seconds.

Adding the 15 seconds for venous transit (times vary greatly with the distance from the heart and the flow in the particular vein selected for the intravenous catheter) to the 20 seconds for central circulation transit, one can appreciate the concept of arm-brain circulation time, which is empirically spoken of among anesthesiologists as being approximately one-half minute. Again, there will be an additional 9 seconds or so added to time required to see the initial thiopental response due to the very long length of intravenous tubing leading from the "injection room" to the "death chamber."

In the fluid medium of the body, drug diffuses from areas of high concentration to adjacent areas where the concentration is lower. During the onset of effect, thiopental diffuses from the blood where the concentrations become quite high, after the initial 35 seconds required for transit, into the brain where the thiopental concentration starts at zero. Without continued thiopental administration, diffusion continues in this direction for approximately 2.5 minutes, at which time blood and brain concentrations are momentarily equal. Then diffusion reverses direction and the drug begins to move from the brain back into the blood. Brain concentrations will continue to fall at a rate governed by the decrease in blood concentrations since brain concentrations will never fall below those of the blood during this phase. Figure 1 depicts the probability of unconsciousness or burst suppression as a function of the brain concentration of thiopental.

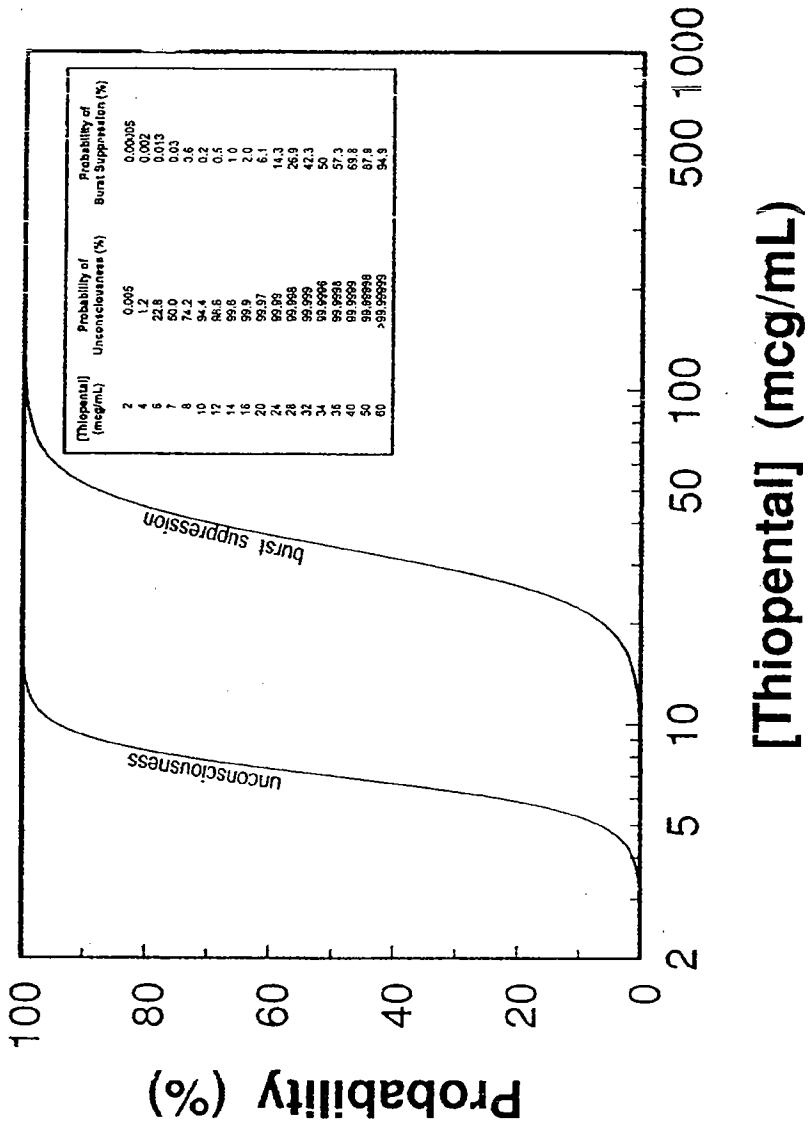

Figure 1: The probability that a person will experience unconsciousness or burst suppression on the EEG as a function of the brain concentration of thiopental. Note that the x-axis is shown as a logarithmic scale for clarity.[16]

16. *See, e.g., supra* note 4 and accompanying text.

R

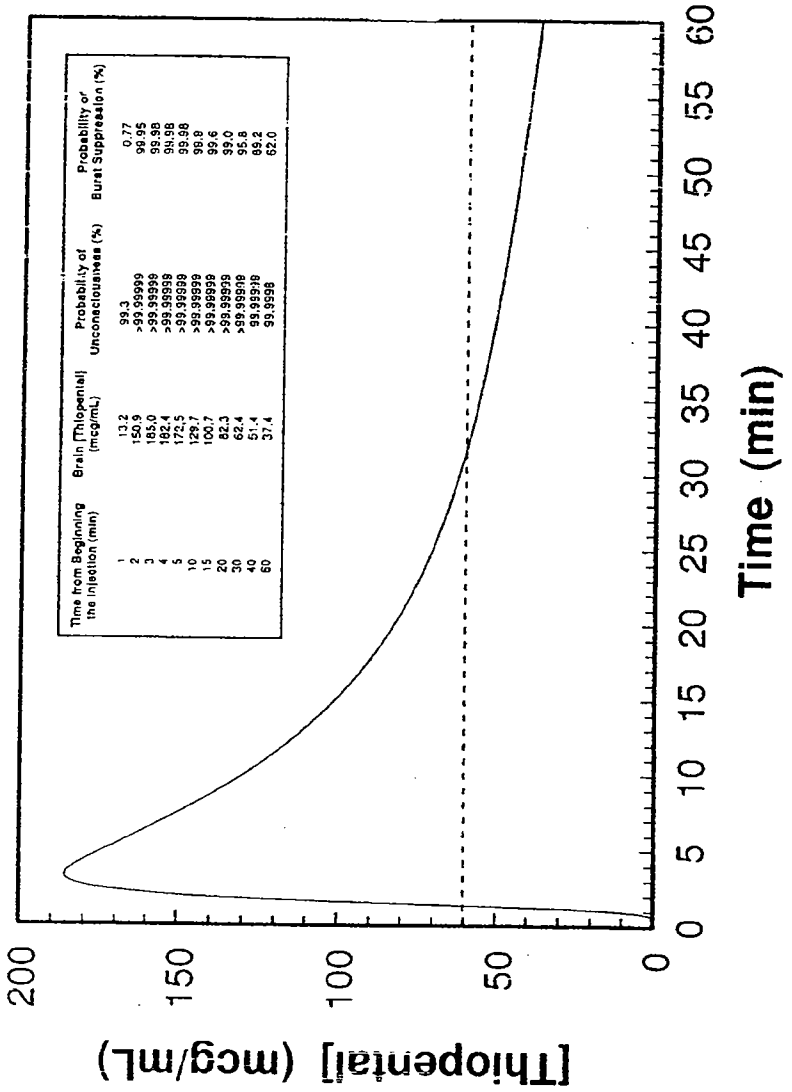

Figure 2: The predicted brain concentration of thiopental following the administration of a dose of 5000 mg given at a rate of 167 mg/sec to an average 80-kg person. The dashed line indicates the brain concentration above which 95% of persons will experience burst suppression on the EEG.[17]

17. *See* Dershwitz & Rosow, *supra* note 6, at 850.

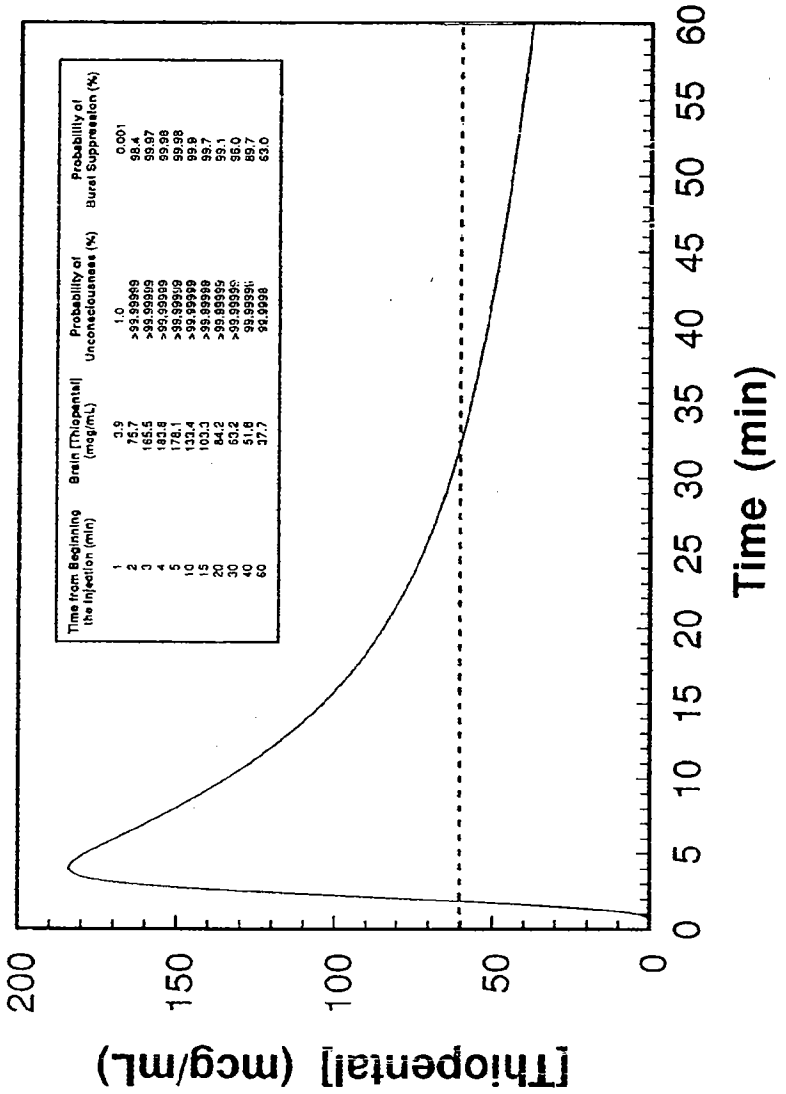

Figure 3: The predicted brain concentration of thiopental following the administration of a dose of 5000 mg given at a rate of 50 mg/sec to an average 80-kg person. The dashed line indicates the brain concentration above which 95% of persons will experience burst suppression on the EEG.[18]

18. The pharmacodynamic model for unconsciousness is in Telford et al., *supra* note 4, at 523-29. See Shanks et al., *supra* note 4, at 309-21 for the pharmacodynamic model for burst suppression. R

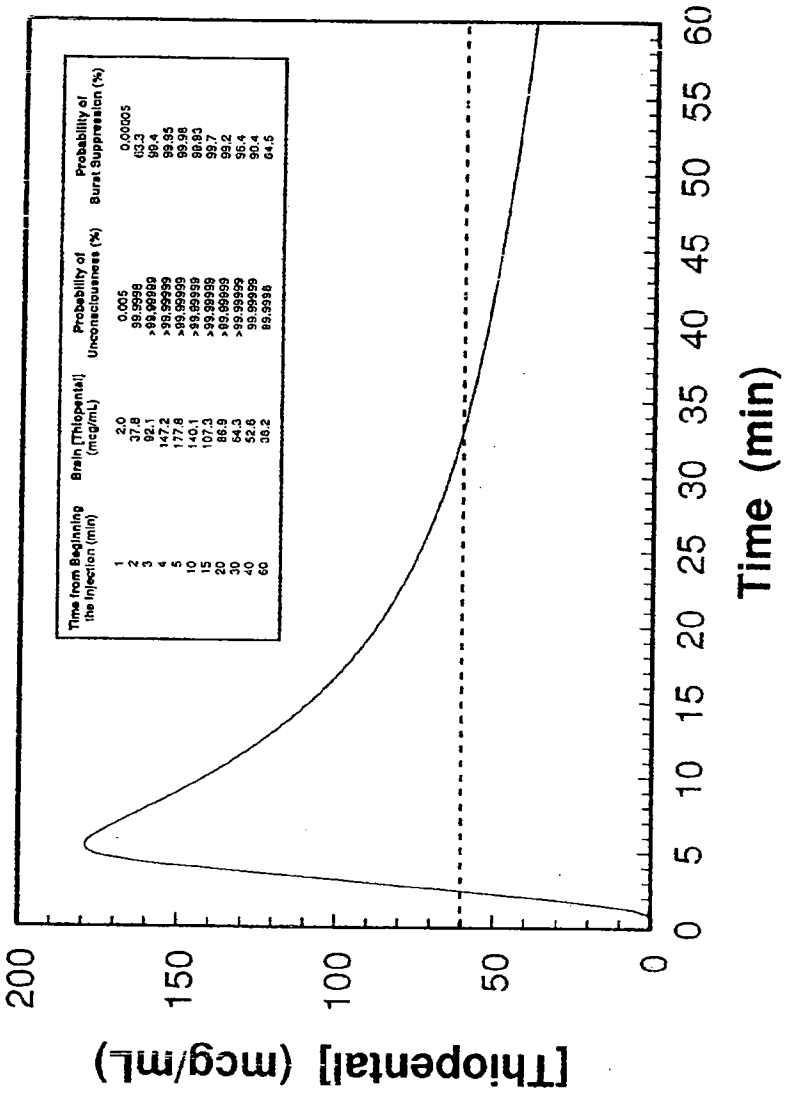

Figure 4: The predicted brain concentration of thiopental following the administration of a dose of 5000 mg given at a rate of 25 mg/sec to an average 80-kg person. The dashed line indicates the brain concentration above which 95% of persons will experience burst suppression on the EEG.[19]

19. The pharmacokinetic model for thiopental used in Figures 2-8 is in Shanks et al., *supra* note 4, at 309-21.

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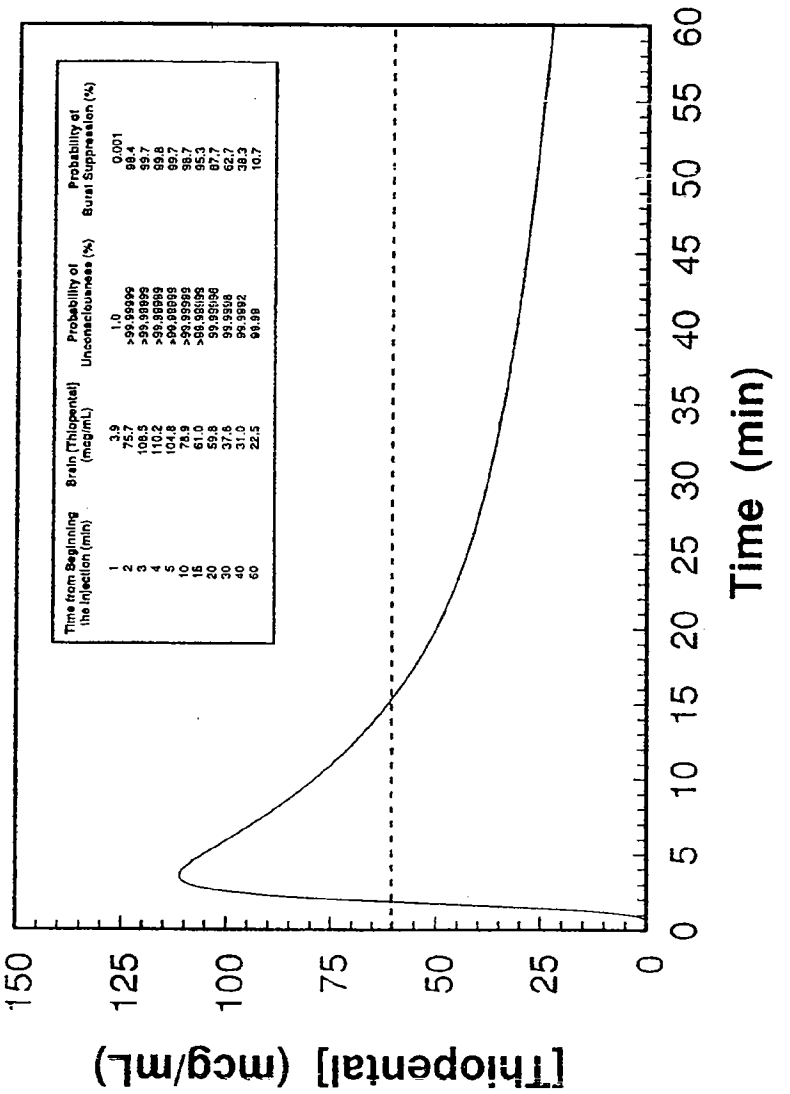

Figure 5: The predicted brain concentration of thiopental following the administration of a dose of 3000 mg given at a rate of 50 mg/sec to an average 80-kg person. The dashed line indicates the brain concentration above which 95% of persons will experience burst suppression on the EEG.[20]

20. *See id.*

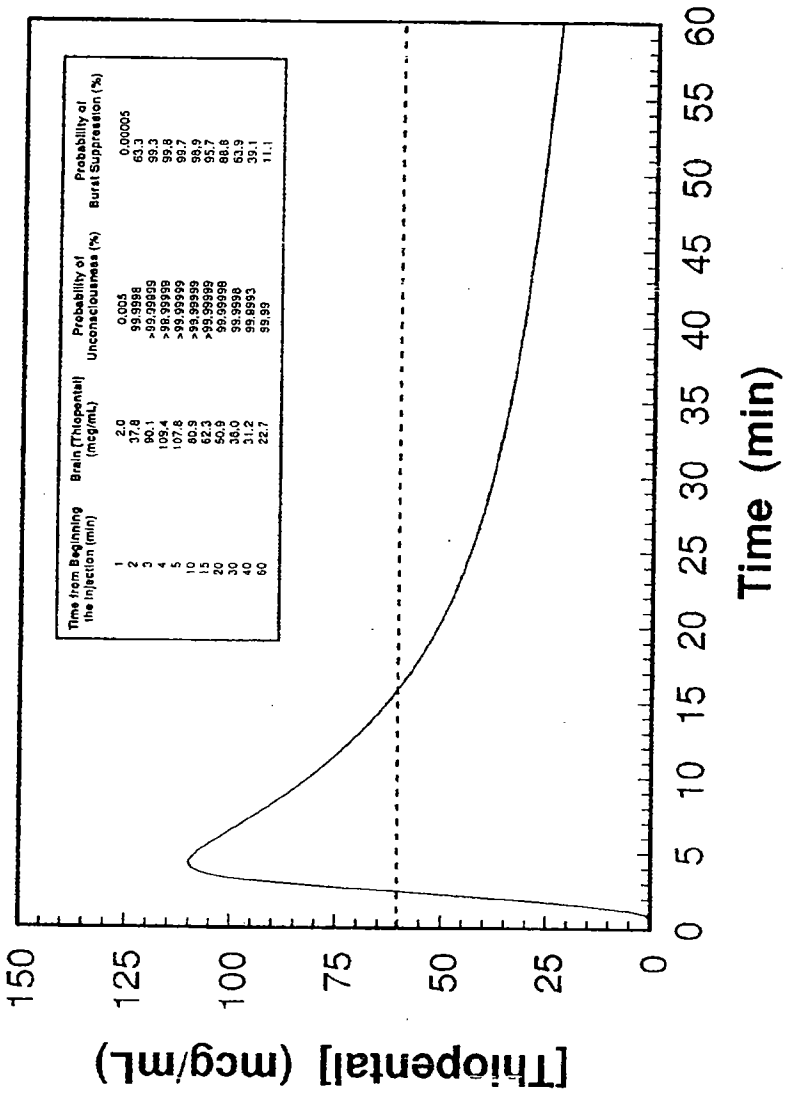

Figure 6: The predicted brain concentration of thiopental following the administration of a dose of 3000 mg given at a rate of 25 mg/sec to an average 80-kg person. The dashed line indicates the brain concentration above which 95% of persons will experience burst suppression on the EEG.[21]

21. *See id.*

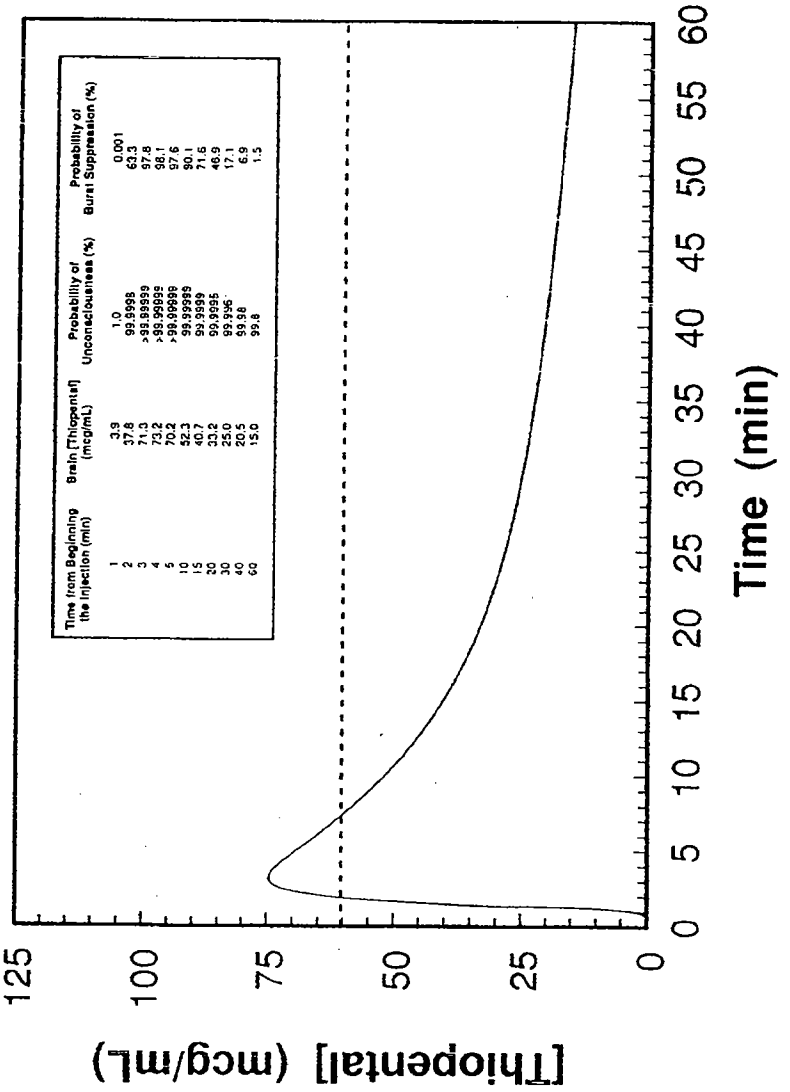

Figure 7: The predicted brain concentration of thiopental following the administration of a dose of 2000 mg given at a rate of 50 mg/sec to an average 80-kg person. The dashed line indicates the brain concentration above which 95% of persons will experience burst suppression on the EEG.[22]

22. *See id.*

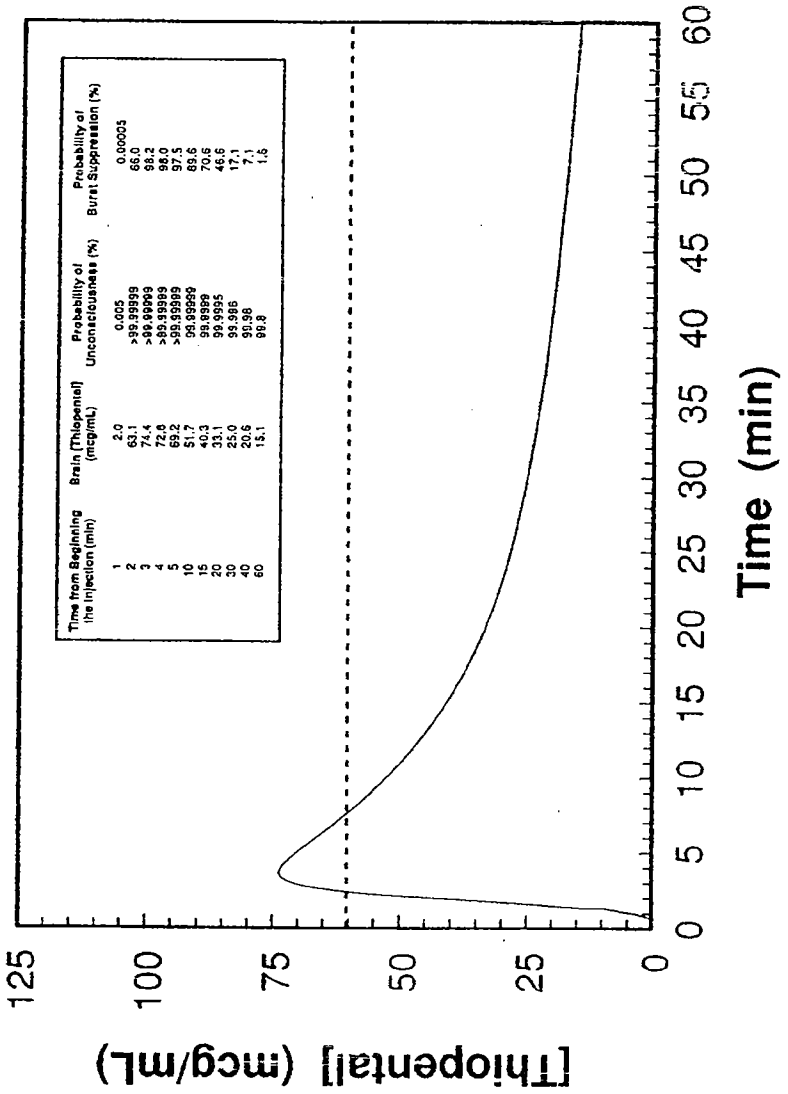

Figure 8: The predicted brain concentration of thiopental following the administration of a dose of 2000 mg given at a rate of 25 mg/sec to an average 80-kg person. The dashed line indicates the brain concentration above which 95% of persons will experience burst suppression on the EEG.[23]

23. *See id.*

Injection Rate (mg/sec)	Time to 95% probability of unconsciousness (min, normal C.O.)	Time to 95% probability of burst suppression (min, normal C.O.)	Time to 95% probability of unconsciousness (min, C.O. ↓ by 75%)	Time to 95% probability of burst suppression (min, C.O. ↓ by 75%)
25	1.6	2.6	2.3	3.1
50	1.4	2.1	2.0	2.7
167	1.1	1.5	1.8	2.2

These principles along with published data regarding the timing of drug onset can be used to construct models to simulate the onset of thiopental effect from any given dose or injection speed.[24] Figures 2 to 8 depict the onset of thiopental effect to the endpoints of unconsciousness and burst suppression for 2000 mg, 3000 mg, and 5000 mg doses at varying injection speeds. Since the onset of effect is rate-limited by blood circulation and diffusion, injection speed matters little. The table above shows the times required, from the beginning of the injection process, to reach a 95% probability of unconsciousness or burst suppression as a function of the injection rate for a 5000-mg dose. The standard solution of thiopental as used clinically is a 2.5% solution, or 25 mg/mL.[25] Therefore, injecting this solution at a rate of 1 mL/sec or 2 mL/sec yields injection rates of 25 mg/sec and 50 mg/sec, respectively. An injection rate of 167 mg/sec (6.7 mL/sec) is achieved by administering a 5000-mg dose over 30 seconds.

Since a 5000-mg dose of thiopental is expected to produce a substantial decrease in the cardiac output (C.O.),[26] the table also shows how the times to reach a 95% probability of unconsciousness or burst suppression are prolonged by a 75% decrease in cardiac output.

II. The Duration of Thiopental Following Various Doses

We shall now consider the *duration* of the effect of the thiopental once it has been administered. The duration of its action should exceed the amount of time required to administer the remaining

24. *See id.*
25. *See id.*
26. *See infra* notes 28-29 and accompanying text.

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medications as well as the time required for the potassium chloride to stop the inmate's heart and to cause his or her death.

The amount of time required to administer all of the medications will depend on the doses specified by the protocol as well as the speed of the injection (i.e. how rapidly the executioner injects each syringe) as well as allowing some time to change syringes by removing one from the intravenous tubing and replacing it with the next one. The following hypothetical three-drug protocol involves using doses at the high end of those used by the various states:

- thiopental, 5000 mg (25 mg/mL, 200 mL)
- saline flush, 50 mL
- pancuronium, 100 mg (1 mg/mL, 100 mL)
- saline flush, 50 mL
- potassium chloride, 240 mEq (2 mEq/mL, 120 mL)
- saline flush, 50 mL

The largest commercially-available syringes used in medicine are 60 mL. The above protocol therefore requires eleven syringes. Assuming ten seconds for each syringe change, the total time to change syringes is 100 seconds. Considering the size of the syringes used (it becomes harder to push the plunger of a syringe as its diameter increases) and the length of the intravenous tubing required to go from the "injection room" to the "death chamber," it is difficult to inject such syringes at a rate greater than 2 mL/sec (or 50 mg/sec when the standard 2.5% solution is used). On the other hand, there is no reason to inject more slowly than 1 mL/sec, so the total volume of the drugs and flushes as listed above, 570 mL, should require no more than approximately eleven minutes to inject.

The potassium chloride should cause cessation of cardiac electrical activity within two minutes of its injection (although see below for a discussion on the effects of thiopental on cardiac output). Therefore, a time period of fifteen minutes should be more than enough to complete an execution, from the beginning of the injection of the thiopental until cessation of electrical activity. Some states mandate a period of time, e.g. five minutes, of continuous electrical inactivity on the electrocardiogram ("ECG"), but that additional time does not need to be considered here.[27]

27. North Carolina, for example, requires such a five-minute period of electrical inactivity prior to the pronouncement of death. *See* North Carolina Department of Correction, Execution Method, http://www.doc.state.nc.us/dop/deathpenalty/method.htm (last visited Apr. 15, 2008).

Figures 2 through 4 depict the predicted concentration of thiopental in the brain following a dose of 5000 mg given at various rates of injection. Referring to Figures 2 to 4, it is apparent that fifteen minutes following the beginning of the thiopental injection, an average person will have essentially a 100% probability of being unconscious and having burst suppression on the EEG. These probabilities are not affected by the speed of the injection.

Figures 5 and 6 depict the predicted brain concentration of thiopental following a dose of 3000 mg given at a rate of 25 mg/sec (1 mL/sec) or 50 mg/sec (2 mL/sec). Fifteen minutes following the beginning of the thiopental injection, an average person will have essentially a 100% probability of being unconscious and about a 95% probability of having burst suppression on the EEG. These probabilities are not affected by the speed of the injection.

Figures 7 and 8 depict the predicted brain concentration of thiopental following a dose of 2000 mg given at a rate of 25 mg/sec (1 mL/sec) or 50 mg/sec (2 mL/sec). The 2000-mg dose of thiopental requires less time to inject than the 5000-mg dose (40 seconds vs. 100 seconds using an injection rate of 50 mg/sec). It will also have a lesser effect in decreasing cardiac output permitting the potassium chloride to circulate more quickly. With the 2000-mg dose, the time required to complete the injection and achieve cardiac arrest will be approximately 7 to 10 minutes with injection rates of 25-50 mg/sec and an additional two minutes to observe cardiac arrest on the ECG. At these time points, a person will have essentially a 100% probability of being unconscious, and a 90-95% probability of having burst suppression on the EEG.

III. Other Effects of Thiopental

The aforementioned predictions of duration of unconsciousness are based upon the persons continuing to breathe (or have their breathing assisted as during surgery). The doses of thiopental used in lethal injection will cause most persons to stop breathing and to have their blood pressures substantially decreased.[28] Thus, even in the absence of the administration of pancuronium and/or potassium chloride, doses of thiopental of 2000 mg and above will be lethal in most persons due to the impairment of delivery of oxygen to critical organs such as the heart and brain. The largest dose of thiopental used in clinical medicine, about 3000 mg, is occasionally used for "brain protection" when there is the planned and deliber-

28. *See generally*, Dershwitz & Rosow, *supra* note 6, at 853. R

ate interruption of blood flow to the brain.[29] Such an interruption of blood flow may occur during certain brain surgeries to repair an aneurysm or arteriovenous malformation. During such surgical procedures, patients are mechanically ventilated so that the effect of thiopental on ventilation is not relevant. However, a dose of 3000 mg of thiopental will decrease the cardiac output and the blood pressure to a dramatic, and dangerous, degree. Such patients require the aggressive administration of medications to maintain adequate blood pressure and oxygen delivery to organs. While neither of us, nor any other physician we know, has ever given a 3000-mg dose of thiopental to a patient who was not mechanically ventilated nor had his or her circulation supported, it is difficult for us to imagine that the administration of 3000 mg of thiopental to an inmate, by itself, is survivable.

We are unaware of any indication in clinical medicine in which a 5000-mg dose of thiopental is given to an 80-kg patient. The negative cardiac effects of such a huge dose of thiopental are necessarily larger than those following a 3000-mg dose. In fact, there is circumstantial evidence that a 5000-mg dose of thiopental may have caused, in some inmates, virtual cessation of the circulation. California is one of the states that uses a 5000-mg dose of thiopental as well as an ECG to monitor the electrical activity of the heart. There have been several executions in California in which a second dose of potassium chloride was given, as mandated by the protocol, because cessation of electrical activity on the ECG did not occur after the first dose.[30] One possible explanation is that the potassium chloride was not injected through a working intravenous catheter. Another more plausible explanation is that the potassium chloride did not circulate to the heart from the site of the intravenous injection.

IV. Assessing the Presence or Absence of Consciousness

As previously described, all of the lethal injection protocols that we have reviewed are intended to render the inmate unconscious prior to the administration of pancuronium and potassium chloride

29. *See* W.A. Kofke, *Protection of the Central Nervous System in Surgical Patients*, in ANESTHESIOLOGY, *supra* note 3, at 1939-40.

30. For example, the execution log of Robert L. Massey, who was executed on March 27, 2001, indicates he was given a second dose of potassium chloride five minutes after the first dose failed to produce a flat ECG, and the execution log of Stephen Wayne Anderson who was executed on January 29, 2002, indicates he was given a second dose of potassium chloride four minutes after the first dose failed to produce a flat ECG.

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and to maintain unconsciousness until death occurs.[31] The greatest risk to the inmate, in terms of the humaneness of an execution, is the administration of pancuronium and/or potassium chloride to an inmate who is conscious. Based upon the history of those executions that did not go as intended, the most frequent problem in such executions has been an intravenous catheter that was not actually within a vein.[32]

If the intravenous catheter was not positioned correctly from the beginning, all of the medications will be delivered to the subcutaneous tissues and the inmate will not lose consciousness as rapidly as expected. A less plausible, but still possible, scenario is one in which the thiopental is delivered subcutaneously but then the intravenous catheter begins functioning properly and the remaining medications are delivered intravenously. In such a scenario, the inmate could be conscious and experience the paralytic effects of pancuronium and the pain associated with the injection of potassium chloride.

Such a risk could be lessened if the inmate were demonstrated to be unconscious following the administration of thiopental and before the administration of the pancuronium and potassium chloride. This sort of assessment is mandated by some protocols and makes use of either a physical examination or an EEG monitor.[33]

Assessing the *depth* of anesthesia is a complex examination requiring both significant training and experience, which is obligatory in clinicians who administer anesthesia. Assessing the *presence of unconsciousness*, in contrast, is something many paramedical personnel do routinely. Such an examination typically involves the application of graded stimuli and the assessment of the response to:

- a spoken command (e.g. "open your eyes")
- a tactile reflex (e.g. gently stroking an eyelash)
- gentle shaking
- a noxious stimulus (e.g. a strong pinch)

31. *See supra* note 2 and accompanying text. R

32. The executions of Joseph Clark on May 2, 2006, in Ohio and of Angel Diaz on December 13, 2006, in Florida were characterized by prolonged periods following the administration of thiopental during which the inmates did not lose consciousness as would have been expected had the medication been introduced intravenously.

33. For example, the protocols used by Missouri and the federal government include an assessment of consciousness by physical examination. The protocol used by North Carolina employs a type of EEG monitor. *See, e.g.*, Connor v. N.C. Council of State, Nos. 07-GOV-0238, 07-GOV-0264 (N.C.O.A.H. Aug. 9, 2007) (describing North Carolina's lethal injection protocol).

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The lack of any response to these graded stimuli is strong evidence that a person is indeed unconscious.

One state, North Carolina, uses the bispectral index ("BIS") monitor in its lethal injection protocol.[34] This is a type of EEG monitor commonly used by anesthesiologists to assess the depth of anesthesia and decrease the incidence of intraoperative awareness.[35] It involves placing an electrode array on the forehead and connecting these electrodes to the monitor. Although the monitor displays much neurophysiological information, the parameter of greatest interest is the bispectral index, or BIS. This is a dimensionless number that ranges from zero to 100.[36] Zero corresponds to complete electrical inactivity of the EEG (i.e. "flatline") while 100 corresponds to the completely awake state.[37] Many clinical studies have shown that a BIS value of 40-60 is associated with a clinically appropriate depth of anesthesia and a very low probability of intraoperative awareness.[38]

North Carolina has utilized the BIS monitor in several executions. The monitor is viewed by a nurse. The executioner pauses after the administration of thiopental (3000 mg in this state) and awaits a signal from the nurse before giving the pancuronium and potassium chloride. In each execution in which it has been used, the BIS value was 0-10 *before* the thiopental administration was complete.

V. Postmortem Determination of Thiopental

Some states routinely perform autopsies on executed inmates and such autopsies may include drawing blood for the measurement of the thiopental concentration.[39] Unfortunately, in far too many of these autopsies the blood samples have been improperly

34. *See id.*; Brown v. Beck, 2006 U.S. Dist. LEXIS 60084, at *4 (E.D.N.C. Apr. 7, 2006).

35. *See* Paul S. Myles et al., *Bispectral Index Monitoring to Prevent Awareness During Anaesthesia: The B-Aware Randomised Controlled Trial*, 363 Lancet 1757, 1757 (2004); Y. Punjasawadwong et al., *Bispectral Index for Improving Anaesthetic Delivery and Postoperative Recovery*, 1 The Cochrane Library 1, 2 (2008) (reprinted by The Cochrane Collaboration).

36. *See* Lee A. Kearse et al., *Bispectral Analysis of the Electroencephalogram Predicts Conscious Processing of Information During Propofol Sedation and Hypnosis*, 88 Anesthesiology 25, 25-34 (1998).

37. *Id.*

38. *See* Myles et al., *supra* note 35, at 1757, 1763; Punjasawadwong et al., *supra* note 35, at 6. R R

39. Leonidas G. Koniaris et al., *Inadequate Anaesthesia in Lethal Injection for Execution*, 365 Lancet 1412, 1412-14 (2005).

obtained and the results have therefore been erroneously interpreted.

Thiopental undergoes postmortem redistribution. This means that the blood concentration of thiopental continues to decrease even after the inmate's death and the cessation of circulation.[40] There is unfortunately very little information on the postmortem kinetics of thiopental because historically thiopental has been of little importance to forensic toxicologists. There are no peer-reviewed papers in the medical literature that have evaluated the postmortem redistribution of thiopental. Medical examiners in several jurisdictions have drawn paired blood samples following executions in order to assess the presence and degree of postmortem redistribution.[41] The first blood sample was obtained soon after the execution, while the second blood sample was obtained hours later at the time of autopsy. We are aware of the following sets of paired blood samples that demonstrate that postmortem redistribution of thiopental does indeed occur:

Jurisdiction	Inmate	Date	[Thiopental] mcg/mL Obtained soon after death	[Thiopental] mcg/mL Obtained at autopsy
CT	Ross	5/13/05	29.6	9.7
NC	McHone	11/11/05	21	1.5
NC	Syriani	11/18/05	12	4.4
NC	Boyd	12/2/05	29	11
NC	Simpson	1/20/06	42	12
MT	Dawson	8/11/06	21	3

In each case, "soon" after death means that the blood sample was drawn within an hour of completing the execution. Autopsies were performed at various times following the executions, ranging from about seven to eighteen hours.

Some persons have argued that this table represents nothing more than a group of random numbers.[42] There are indeed *pooled* data that are purported to demonstrate no time-dependent de-

40. *See* A.L. Pélissier-Alicot et al., *Mechanisms Underlying Postmortem Redistribution of Drugs: A Review*, 27 J. ANAL. TOXICOL. 533, 533-44 (2003).

41. Such postmortem analyses have been performed following executions in Connecticut, Montana, and North Carolina.

42. *See generally* Susi Vassallo, *Thiopental In Lethal Injection*, 35 FORDHAM URB. L.J. 957 (2008); Teresa A. Zimmers & Leonidas Koniaris, *Peer-reviewed Studies Iden-*

crease in the thiopental concentration in blood following death.[43] The table above is, however, the only example of *paired* data in which blood samples were drawn from the *same* inmate at *different* times following death. Applying Student's t-test for paired data to the data in the above table yields a p value of 0.0013. The interpretation of this statistical result is that there is a 99.9987% probability of a significant *decrease* in the blood thiopental concentration as a function of time following death by lethal injection where death closely follows a single rapid infusion of the drug and pseudoequilibrium with the majority of the body's tissues did not have time to be completed.[44] These data confirm the process of postmortem redistribution and would suggest that a rise in blood thiopental concentrations would be seen if similar paired postmortem samples were obtained when death occurred much longer after a dose of thiopental (as might occur in a clinical situation) at a time well after pseudoequilibrium between blood and tissue drug concentrations when the concentration gradient would be expected to be reversed.

In addition to the process of postmortem redistribution, another possible source of misleading postmortem thiopental data is the difference in the concentration of thiopental in arteries and veins. Pathologists most commonly draw postmortem blood samples from the femoral vein in the groin. Located immediately next to the femoral vein is the femoral artery. During life, it is usually easy to locate the femoral artery because it is typically the strongest peripheral pulse in the body. Following death, this landmark is lost. Since the femoral vein has a greater diameter, when a needle is inserted blindly in the groin, the femoral vein is more likely to be entered. However, Figure 9 shows that there may be substantial and clinically meaningful differences between the arterial and venous concentrations of thiopental. Assuming a normal cardiac output, differences between the arterial and venous concentrations of thiopental are expected for approximately four minutes following the beginning of thiopental administration. In contrast, if thiopental were to cause a large decrease in cardiac output (as is expected with the large doses used in lethal injection protocols), the differ-

tifying Problems in the Design and Implementation of Lethal Injection for Execution, 35 FORDHAM URB. L.J. 919 (2008).

43. *See* Koniaris et al., *supra* note 39, at 1412-14; Teresa A. Zimmers et al., *Authors' Reply, Inadequate Anaesthesia in Lethal Injection for Execution*, 366 LANCET 1073, 1074-76 (2005). R

44. *See* Stanton Glantz, PRIMER OF BIOSTATISTICS 322-25 (McGraw-Hill, 6th ed. 2005).

ence in the arterial and venous concentrations will persist until well after the expected occurrence of death.

The accurate differentiation between the femoral artery (lacking a pulse) and the femoral vein following death requires dissection and visualization of both vessels. Many medical examiners are unwilling to perform such a procedure at a prison on an inmate who has just been executed. Were a state to decide that the acquisition of a blood sample from a known blood vessel is a prudent idea, they might consider hiring a funeral director to perform the procedure. Since the process of embalming involves dissection and visualization of arteries and veins so that the embalming fluid can be injected, funeral directors should readily be able to obtain accurately femoral arterial and femoral venous blood for analysis.

We believe that there should be as much transparency as possible in the lethal injection procedure. Therefore, we support the practice of obtaining postmortem blood samples for thiopental analysis as a routine procedure. It is, however, crucial to obtain the blood sample properly and that means drawing it soon after the inmate's death, preferably within a few minutes and definitely within an hour.

VI. Conclusions

In summary, our pharmacokinetic and pharmacodynamic predictions of the effects of thiopental as used in the lethal injection protocols we have reviewed suggest that these protocols, if implemented as written, will result in the rapid death of the inmate without undue pain or suffering.

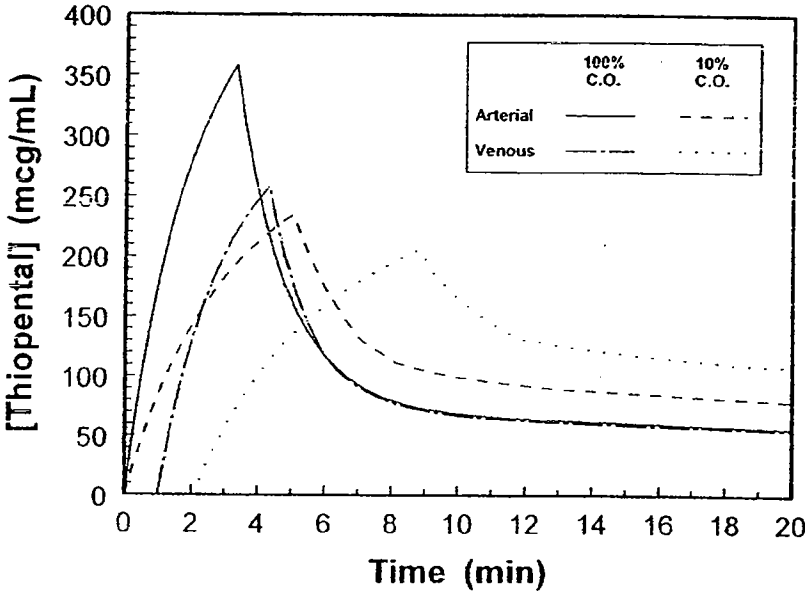

Figure 9: The effect of thiopental-induced decrease in cardiac output on the time course of the arterial and venous concentrations of thiopental. The predicted arterial blood concentration of thiopental following the administration of a dose of 5000 mg given at a rate of 1 mL/sec to an average 80-kg person is depicted by the solid line. The simultaneous venous blood concentration is depicted by (— - —). The two other lines assume a 90% decrement in cardiac output caused by thiopental. The dashed line depicts the predicted arterial concentration, while the dotted line depicts the predicted venous concentration.[45]

Implementing a protocol as written means the correct doses of the correct medications are administered in the correct order into a properly functioning intravenous delivery system and allowing sufficient time for thiopental to produce its effect.

We previously discussed that the cardiovascular and respiratory effects of thiopental given by itself in doses of 2000 mg and above are likely to be lethal in virtually everyone. Much has been written and said about adopting lethal injection protocols that rely on a single drug alone such as thiopental. As clinical pharmacologists, we can describe the advantages and disadvantages in comparing the current three-drug protocol with a protocol consisting of thio-

45. The pharmacokinetic model for thiopental used in Figure 9 is in T.D. Homer & D.R. Stanski, *The Effect of Increasing Age on Thiopental Disposition and Anesthetic Requirement*, 62 ANESTHESIOLOGY 714, 714-24 (1985). Some of the cardiovascular modeling was performed using the program A-ware, Springer Electronic Media.

pental as the only medication. We cannot, however, state which option is "better" because in this context "better" is based not upon pharmacological considerations but is actually a public policy decision best made by well-informed policy makers.

Some persons have contended that a large dose of thiopental given by itself does not reliably produce death.[46] In the Netherlands, where euthanasia and physician-assisted suicide are both legal, the Royal Dutch Society for the Advancement of Pharmacy wrote, "For intravenous administration, thiopental receives most consideration. It is not possible to administer so much of it that a lethal effect is guaranteed, but the substance is quite suitable for producing coma, after which termination may be effected using a muscle relaxant."[47] In the same article, the thiopental dose to be used was stated as, "intravenous administration of 1 g thiopental sodium, if necessary, 1.5-2 g of the product in case of strong tolerance to barbiturates."[48] Apparently the largest dose of thiopental used in the Netherlands was only 2 g (or 2000 mg) and it is therefore not surprising that such a dose was found to be less than 100% lethal.

The primary advantage of the three-drug protocol is that there is a definite and rapid end-point to the protocol and that is the onset of a flat-line ECG that can be assessed remotely by viewing an ECG monitor. The primary disadvantage is that there is the risk that the inmate could experience pain and suffering if the dose of thiopental is not properly administered for whatever reason and the pancuronium and potassium chloride are then administered to a conscious person. Another disadvantage to the three-drug protocol is that the potassium chloride, in addition to its action in stopping the heart, also causes widespread stimulation of nerve and muscle tissue throughout the body. Such stimulation is often manifested as involuntary muscle contractions that may have in the past been misperceived by lay witnesses as consistent with pain or suffering, or experiencing a seizure. In fact, it is most unlikely that someone given a large dose of thiopental, an excellent anticonvulsant medication, could suffer a seizure. One action of the pancuronium is to mitigate these involuntary muscle contractions.

46. Teresa A. Zimmers et al., *Lethal Injection for Execution: Chemical Asphyxiation?* 4(4) PLoS MEDICINE 646, 646-47 (2007).

47. For an English translation of the article, see *Administration and Compounding of Euthanasic Agents*, The Hague (Royal Dutch Society for the Advancement of Pharmacy 1994), *available at* http://wweek.com/html/euthanasics.html.

48. *Id.*

The primary advantage of a protocol in which a large dose of thiopental is given by itself is that there is no risk whatsoever of the inmate experiencing pain or suffering due to the effects of pancuronium or potassium chloride. If the intravenous catheter were to malfunction and the thiopental were deposited next to, instead of inside of, the vein, the inmate might experience some pain at the injection site but in fact this is a potential risk to which any patient given thiopental for anesthesia is subjected. The primary disadvantage of this single-drug protocol is that, although the inmate will likely die within a few minutes, his death will not be immediately reflected on the ECG monitor. In fact, following a large dose of thiopental that causes the inmate to stop breathing, experience a huge drop in blood pressure, and therefore a fatal decrease in oxygen delivery to critical tissues, it might very well take a half hour or longer for the ECG to become flat. In this case, it would be imprudent to wait for the ECG to become flat, and death would need to be ascertained by a physical examination that demonstrated the absence of a heartbeat or evidence of circulation. Whether this physical examination is performed by a physician or a paraprofessional credentialed to pronounce death (such as a nurse or a paramedic), either the person would be visible to the witnesses or the curtains in the death chamber would need to be drawn for the pronouncement of death to maintain this person's anonymity. Once again, we are unable to state, based upon pharmacological principles, which of these options is "better," however, we believe that those policy makers responsible for making such decisions are entitled to accurate scientific information in order to make an informed policy decision.

EXHIBIT 11

DECLARATION OF FIONA JANE COUPER, Ph.D

I, FIONA JANE COUPER, make the following declaration:

1. I am over the age of eighteen years and am competent to testify to the matters set forth below.

2. I am employed as the Washington State Toxicologist. I have held this position since March 2008. My professional and educational qualifications are set forth in my curriculum vitae, a copy of which is provided as Attachment A to this declaration. As the Washington State Toxicologist, I oversee the Toxicology Laboratory Division, which includes a staff of 16 full time toxicologists and provides drug and alcohol testing for coroners, medical examiners, law enforcement agencies, and prosecuting attorneys. This position also involves supervision of the Washington State Patrol's Impaired Driving Section, consisting of the Breath Test Program, Drug Recognition Program and the Ignition Interlock Program. This involves overseeing the training and certification of technicians, operators and instructors, and the approval of all policies and procedures. I am also responsible for the supervision of the blood alcohol analyst program for Washington State, and I provide expert testimony on the effects of alcohol and drug intoxication, driving under the influence of alcohol and/or drugs, and blood and breath testing for alcohol and drugs.

3. I have reviewed the Department of Corrections Policy Directive 490.200, Capital Punishment, effective October 25, 2008.

4. Thiopental sodium is an ultra-short acting barbiturate typically used as an anesthetic and/or induction agent. It induces a deep, coma-like unconsciousness within 30-60 seconds, and typical anesthetic/induction doses are approximately 100-250 mg, rarely more than 1 gram. Following a 3 gram dose, respiratory functions would be significantly depressed or stopped within approximately one to two minutes. While unconscious, the subject would have no sense of physical pain or suffering.

EXHIBIT H

5. Pancuronium bromide is a neuromuscular blocking agent (paralytic agent). It inhibits muscular-skeletal movements thereby paralyzing the diaphragm and other respiratory muscles, and stopping respiration. Typical therapeutic doses are 0.04-0.10 mg/kg. At a 100 mg dose, respiratory paralysis should occur within 30-60 seconds of administration. Additionally, the heart would stop beating within approximately one to three minutes.

6. Potassium chloride is a chemical compound that interferes with the electrical signals that stimulate the contractions of the heart. A dose of 240 mEq would be sufficient to cause death by cardiac arrest within approximately one to three minutes.

7. Based on my professional experience and review, it is my opinion that the proper administration of the three drugs listed under Section IX.A.4(d) of the policy, in the sequence and dosages specified, would be a fatal combination resulting in a swift and painless death.

8. It is my professional opinion that flushing the intravenous (IV) lines with 50 cc of normal saline solution after the administration of each of the first two drugs specified (thiopental sodium and pancuronium bromide) should prevent clogging in the IV lines.

I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge.

Signed this 7th day of November, 2008, at Seattle, Washington.

FIONA JANE COUPER, Ph.D.

ATTACHMENT A

CURRICULUM VITAE
July 2008

FIONA JANE COUPER

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EMPLOYMENT

Mar 2008 - present — **State Toxicologist, Toxicology Laboratory Division Commander**
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Nov 2001 - Feb 2008 — **Chief Toxicologist, Director of Laboratory Services**
Toxicology Laboratory
District of Columbia, Office of the Chief Medical Examiner
Dr. Marie Pierre-Louis (Chief Medical Examiner)
Washington, D.C. U.S.A.

Sept 1998 - Oct 2001 — **Senior Fellow - Post Doctoral Fellowship and Forensic Toxicologist**
Department of Laboratory Medicine, University of Washington
Washington State Toxicology Laboratory
Dr. Barry K. Logan (Director, Forensic Laboratory Services Bureau)
Seattle, WA U.S.A.

April 1997 - Aug 1998 — **Research Fellow - Post Doctoral Fellowship**
National Institute of Forensic Science
Victorian Institute of Forensic Medicine
A/Professor Olaf H. Drummer (Head, Scientific Services)
Melbourne VIC, Australia

July 1994 - Dec 1994 — **Research Assistant 3 (Part time)**
Department of Social and Preventive Medicine
Caulfield General Medical Centre
Dr. Malcolm R. Sim (Head, Senior Lecturer)

ATTACHMENT A

Caulfield VIC, Australia

Nov 1992 - Aug 1998 **Forensic Toxicologist VPS 2 (Part time)**
Department of Forensic Medicine
Victorian Institute of Forensic Medicine
Dr. Iain M. McIntyre (Toxicology Laboratory Manager)
Melbourne VIC, Australia

EDUCATION

1989-1991 **Bachelor of Science,**
Faculty of Science, Monash University, Australia
Majors: Pharmacology-Toxicology, Biochemistry

1992 **Bachelor of Science (Honours)**, Pharmacology-Toxicology
Department of Pharmacology, and Department of Forensic Medicine
Monash University, Australia
Thesis: *Detection of Antidepressants and Antipsychotics in Human Scalp Hair*

1993-1997 **Doctor of Philosophy, Ph.D. (Med)**, Forensic Medicine-Forensic Toxicology
Department of Forensic Medicine, Monash University, Australia
Thesis: *The Involvement of β_2-Agonists in Asthma Deaths*

TEACHING EXPERIENCE, RESEARCH SUPERVISOR

1992 Pharmacology/Toxicology Laboratory Assistant
Department of Pharmacology, Monash University

1997 Research Co-supervisor – Karen van Loon, B.Sc. (Hons)
Department of Forensic Medicine, Monash University, Australia
Department of Pharmacy, University of Groningen, Netherlands

1999-2001 Lecturer – Medical Technology (Chemistry), LMED 322, 418
Department of Laboratory Medicine, University of Washington

1999-2001 Faculty Mentor/Supervisor – Senior Research Enrichment Program
Department of Laboratory Medicine, University of Washington

2002-2005 Instructor – The Effects of Drugs on Human Performance and Behavior
Robert F. Borkenstein Center for Studies of Law in Action
Department of Criminal Justice, Indiana University

PROFESSIONAL SOCIETIES, COMMITTEES

1992-1998 Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists
1993-1997 Victorian Asthma Mortality Study Group - Steering Committee
1994- present The International Association of Forensic Toxicologists (TIAFT)
1997-1999 TIAFT – member; Young Scientists Committee (Asia-Pacific Regional Representative)
1998- present Society of Forensic Toxicologists (SOFT)
1998- present American Academy of Forensic Sciences (AAFS)
1999-2001 Seattle King County - Community Epidemiology Working Group (NIDA-CEWG)
1999- 2003 TIAFT – member; Young Scientists Committee (U.S.A. Regional Representative)
1999- present SOFT – member; Drug-Facilitated Sexual Assault Committee
2000 International Consultative Workgroup on Drugs and Driving Impairment – delegate & rapporteur

2001	Guest reviewer for *Forensic Science Communications*
2001	Guest reviewer for the 2001 *Special Issue of the Journal of Analytical Toxicology*
2001	Guest reviewer for *Journal of Analytical Toxicology*
2001- 2003	Editorial Board for the AAFS Toxicology Section's *News & Views*
2001- present	SOFT/AAFS – member; Joint Drugs and Driving Committee
2002- 2005	SOFT/AAFS – Chair; Joint Drugs and Driving Committee
2002	SOFT member; Nominating Committee
2002	Guest reviewer for the 2002 *Special Issue of the Journal of Analytical Toxicology*
2003	Guest reviewer for *Forensic Science International*
2004	Guest reviewer for the 2004 *SOFT/TIAFT Special Issue of Forensic Science International*
2004	Guest reviewer for the 2004 *Special Issue of the Journal of Analytical Toxicology*
2005	Guest reviewer for the 2005 *Special Issue of the Journal of Analytical Toxicology*
2006	Guest reviewer for the 2006 *Special Issue of the Journal of Analytical Toxicology*
2006 - present	AAFS – member; Toxicology Awards and Scholarships Committee
2006	SOFT Annual Meeting, Scientific Program Chair

SCHOLARSHIPS, AWARDS, FELLOWSHIPS

1993-1996	Monash Graduate Scholarship, Monash University, Australia
1995	Conference Grant-In-Aid Scholarship, Monash University, Australia
1997-1998	National Institute of Forensic Science, Australia - Research Fellowship
1998-2001	University of Washington, U.S.A. - Postdoctoral Fellowship
2004	Paul Coverdell Forensic Science Improvement Grant
2006	Irving Sunshine Award, American Academy of Forensic Sciences

PUBLICATIONS (Peer Reviewed)

1. Extraction of Psychotropic Drugs from Human Scalp Hair

   Couper FJ, McIntyre IM, Drummer OH. *Journal of Forensic Sciences* 1995; 40: 83-86

2. Detection of Antidepressant and Antipsychotic Drugs in Postmortem Human Scalp Hair

   Couper FJ, McIntyre IM, Drummer OH. *Journal of Forensic Sciences* 1995; 40: 87-90

3. Gas Chromatographic-Mass Spectrometric Determination of β_2-Agonists in Postmortem Blood: Application in Forensic Medicine

   Couper FJ, Drummer OH. *Journal of Chromatography* 1996; 685: 265-272

4. Reviewing Mortality

   Abramson M, **Couper F**, Campbell D, and The Victorian Asthma Mortality Study Group. *Clinical Asthma Reviews* 1998; 2: 21-25

5. Postmortem Stability and Interpretation of β_2-Agonist Concentrations

   Couper FJ, Drummer OH. *Journal of Forensic Sciences* 1999; 44 (3): 523-526

6. Determination of γ-Hydroxybutyrate (GHB) in Biological Specimens by Gas Chromatography-Mass Spectrometry

   Couper FJ, Logan BK. *Journal of Analytical Toxicology* 2000; 24: 1-7.

7. Are Asthma Medications and Management Related to Deaths from Asthma?

   Abramson MJ, Bailey M, **Couper F**, Driver JS, Drummer OH, Forbes AB, McNeil JJ, Walters E.H. *American Journal of Respiratory and Critical Care Medicine* 2001; 163: 12-18

8. Zolpidem and Driving Impairment

   Logan BK, **Couper FJ**. *Journal of Forensic Sciences* 2001; 46 (1): 102-107

9. GHB and Driving Impairment

   Couper FJ, Logan BK. *Journal of Forensic Sciences* 2001; 46(4): 151-155.

10. 3,4-Methylenedioxymethamphetamine (MDMA, Ecstasy) and Driving Impairment
Logan BK, **Couper FJ**. *Journal of Forensic Sciences* 2001; 46(6): 1426-1433.
11. Prevalence of Drug Use in Commercial Tractor-Trailer Drivers
Couper FJ, Pemberton M, Jarvis A, Hughes M, Logan BK.
Journal of Forensic Sciences 2002; 47(3): 562-567.
12. γ-Hydroxybutyrate (GHB): Effects on Human Performance and Behavior
Couper FJ, Marinetti L. *Forensic Science Review* 2002; 14(1/2): 101-121.
13. 3,4-Methylenedioxymethamphetamine – Effects on Human Performance and Behavior
Logan BK, **Couper FJ**. *Forensic Science Review* 2003; 15(1): 11-28.
14. Drugs and Human Performance Fact Sheets
Couper F, Logan B. Washington, DC: U.S. Department of Transportation, *NHTSA Technical Report No. DOT HS 809 725*. April 2004.
15. Suspected GHB Overdoses in the Emergency Department
Couper FJ, Thatcher JE, Logan BK. *J Analytical Toxicology* 2004; 28(6): 481-484.
16. Addicted to Driving Under the Influence – a GHB/GBL Case Report
Couper FJ, Logan BK. *J Analytical Toxicology* 2004; 28(6): 512-515.
17. Forensic Applications of New Analytical Technologies
Couper F, Gluodenis T, Jensen M, Klee M, Neufeld L, Quimby B, Zarwell L, Zweigenbaum. *Forensic Magazine* April/May 2005.
18. Substance misuse: Cocaine and other stimulants
Couper FJ. In: *Encyclopedia of Forensic and Legal Medicine*; Elsevier Limited; UK 2005; 141-144.
19. Substance misuse: Sedatives
Couper FJ. In: *Encyclopedia of Forensic and Legal Medicine*; Elsevier Limited; UK 2005; 163-164.
20. Substance misuse: Miscellaneous (volatiles, hallucinogens and 'club' drugs)
Couper FJ. In: *Encyclopedia of Forensic and Legal Medicine*; Elsevier Limited; UK 2005; 165-170.
21. Fatal Methadone Intoxication in an Infant
Couper FJ, Chopra K, Pierre-Louis M. *Forensic Science International* 2005; 153(1): 71-3.

OTHER PUBLICATIONS / PROCEEDINGS

1. Detection of Psychotropic Drugs in Human Scalp Hair
Couper F, McIntyre I, Drummer O. In: Reid JJ, Ching MS (editors). Clinical and Experimental Pharmacology and Physiology (Suppl. 21). Blackwell Scientific, Melbourne, Australia; 1993; 15
2. Method for Quantifying Antidepressant and Antipsychotic Drug Levels in Postmortem Human Scalp Hair
Couper F, McIntyre I, Drummer O. In: Muller K (editor). Contribution to Forensic Toxicology. MolinApress, Leipzig, Germany; 1994; 160-162
3. Detection of Antidepressant and Antipsychotic Drugs in Human Scalp Hair
Couper F, McIntyre I, Drummer O. In: Jacob B, Bonte W (editors). Advances in Forensic Science. Verlag Dr. Koster, Berlin, Germany; 1995; 5: 40-42
4. Toxicological Analysis of Asthmatic Deaths
Couper FJ, Drummer OH. In: Kovatsis AV, Tsoukali-Papadopouou H (editors). Aspects on Forensic Toxicology. Tecnika Studio, Thessaloniki, Greece; 1995; 20-23
5. Blood Salbutamol Levels are Higher in Asthma Deaths than Controls
Abramson M, Driver J, Willis J, Evans N, **Couper F**, Drummer O, McNeil J, Walters E. Proceedings of the National Asthma Conference and Workshop. Melbourne, Australia, 1995
6. Detection of Antidepressant Drugs in Hair
Drummer O, **Couper F**. In: De Zeeuw RA, Hosani IA, Munthiri SA, Maqbool A (editors). Hair Analysis in Forensic Toxicology, Abu Dhabi. 1995; 217-224

7. Extraction of Psychotropic Drugs in Hair

Drummer O, **Couper F**. In: De Zeeuw RA, Hosani IA, Munthiri SA, Maqbool A (editors). Hair Analysis in Forensic Toxicology, Abu Dhabi. 1995; 326-333

8. Toxicological Analysis of Asthmatic Deaths
Couper F, Drummer O. Proceedings of The Australian and New Zealand Forensic Science Society 12th International Symposium on the Forensic Sciences. Sydney, Australia, 1996
9. Blood Salbutamol Levels are Higher in Asthma Deaths than Controls
Abramson M, Driver J, Willis J, Evans N, **Couper F**, Drummer O, McNeil J, Walters E. Proceedings of The Thoracic Society of Australia and New Zealand. Perth, Australia, 1996
10. Blood Salbutamol Levels are Higher in Asthma Deaths than Controls
Coleridge J, Maclean A, Thomson G, Driver J, Willis J, Evans N, **Couper F**, Drummer O, Walters E, Abramson M. Proceedings of The 6th International Conference on Emergency Medicine. Sydney, Australia, 1996
11. Asthma Medications, Blood Salbutamol Levels and Mortality from Asthma
Abramson M, Driver J, Bailey M, Willis J, Evans N, **Couper F**, Drummer OH, Walters EH, Coleridge J, Maclean A, Thomson G. Proceedings of The Thoracic Society of Australia and New Zealand. Wellington, New Zealand, 1997
12. Postmortem Interpretation of β_2-Agonist Concentrations
Couper FJ, Drummer OH. Proceedings of The International Association of Forensic Toxicologists 35th Meeting. Padova, Italy; 1997; 19-25
13. Blood Salbutamol Levels are Higher in Asthma Deaths than Controls after Adjusting for Administration and Severity
Abramson M, Bailey M, **Couper F**, Drummer O, Forbes A, McNeil J, Walters EH. World Asthma Meeting. Barcelona (Spain). Eur Respir J 1998; 12 (Suppl 29): 38s
14. The Application of Hair Analysis to Detect Anabolic Steroid Use in Humans
Couper FJ, Drummer OH. Proceedings of The 14th International Symposium on the Forensic Sciences. Adelaide, Australia, 1998
15. The Involvement of β_2-Agonists in Asthma Deaths
Couper FJ, Drummer OH, Abramson MJ. Proceedings of the American Academy of Forensic Sciences. Orlando FL, U.S.A., 1999
16. Drug-Facilitated Sexual Assault
Couper F. Law Enforcement Digest. Washington, U.S.A., June 1999
17. The Determination of GHB in Clinical and Postmortem Specimens
Couper F, Logan B. Proceedings of the Society of Forensic Toxicologists meeting, Puerto Rico, U.S.A., 1999.
18. Pharmacological Facilitation of Robbery: Analysis of Two Cases from the Emergency Department
Blaho KE, Park LJ, Logan BK, **Couper F**, Winbery SL. Proceedings of the Society of Forensic Toxicologists meeting, Puerto Rico, USA, 1999.
19. Zolpidem and Driving Impairment
Logan BK, **Couper FJ**. Proceedings of the American Academy of Forensic Sciences meeting, Reno NV, U.S.A., 2000.
20. Determination of Drug Use in Tractor-Trailer Drivers: "Operation Trucker Check"
Couper FJ, Anonical A, Pemberton M, Logan BK. Proceedings of the American Academy of Forensic Sciences meeting, Reno NV, U.S.A., 2000.
21. Driving Under the Influence of GHB
Couper FJ, Logan BK. Proceedings of the Society of Forensic Toxicologists meeting, Milwaukee WI, U.S.A., 2000
22. Suspected GHB Overdoses in the Emergency Room
Couper FJ, Thatcher JE, Logan BK. Proceedings of the American Academy of Forensic Sciences meeting, Seattle WA, U.S.A., 2001.
23. A Combined Drug Intoxication Involving Metaxalone (Skelaxin®)
Zarwell LW, Colvin SM, **Couper FJ**. Proceedings of the SOFT-TIAFT-FBI Forensic Toxicology meeting, Washington DC, U.S.A., 2005

PRESENTATIONS (* Invited Speaker)

1. "Detection of Psychotropic Drugs in Human Scalp Hair"
Couper FJ. Presentation at the Department of Pharmacology and Toxicology, Monash University, Melbourne, Australia, October 9, 1992
2. "Detection of Psychotropic Drugs in Human Scalp Hair"
Couper FJ. Presentation at the Australian Society of Clinical and Experimental Pharmacologists and Toxicologists 26th Meeting, Sydney, Australia, December 9, 1992
3. "Method for Quantifying Antidepressant and Antipsychotic Drug Levels in Postmortem Human Scalp Hair"
Couper FJ. Presentation at The International Association of Forensic Toxicologists 31st International Meeting, Leipzig, Germany, August 16, 1993
4. "Detection of Antidepressant and Antipsychotic Drugs in Human Scalp Hair"

Couper FJ. Presentation at the International Association of Forensic Sciences 13th International Meeting, Dusseldorf, Germany, August 23, 1993

5. "Toxicological Analysis of Asthmatic Deaths"
Couper FJ. Presentation at The 33rd International Congress on Forensic (TIAFT) and 1st Environmental Toxicology Meeting, Thessaloniki, Macedonia, Greece, August 31, 1995

6. "Blood Salbutamol Levels are Higher in Asthma Deaths than Controls"
Abramson M, Driver J, Willis J, Evans N, **Couper F**, Drummer O, McNeil J, Walters E. Presentation at the National Asthma Conference and Workshop, Melbourne, Australia, 1995

7. "Detection of Antidepressant Drugs in Hair"
Drummer O, **Couper F**. Presentation at the International Conference and Workshop for Hair Analysis in Forensic Toxicology, Abu Dhabi, November 1995

8. "Extraction of Psychotropic Drugs in Hair"
Drummer O, **Couper F**. Presentation at the International Conference and Workshop for Hair Analysis in Forensic Toxicology, Abu Dhabi, November 1995

9. "Blood Salbutamol Levels are Higher in Asthma Deaths than Controls"
Abramson M, Driver J, Willis J, Evans N, **Couper F**, Drummer O, McNeil J, Walters E. Presentation at the Thoracic Society of Australia and New Zealand meeting, Perth, Australia, March 1996

10. "Blood Salbutamol Levels are Higher in Asthma Deaths than Controls"
Coleridge J, Maclean A, Thomson G, Driver J, Willis J, Evans N, **Couper F**, Drummer O, Walters E, Abramson M. Presentation at the 6th International Conference on Emergency Medicine, Sydney, Australia, May 1996

11. "Toxicological Analysis of Asthmatic Deaths"
Couper FJ. Presentation at The Australian and New Zealand Forensic Science Society 12th International Symposium on the Forensic Sciences, Sydney, Australia, September 10, 1996

12. "Asthma Medications, Blood Salbutamol Levels and Mortality from Asthma"
Abramson M, Driver J, Bailey M, Willis J, Evans N, **Couper F**, Drummer OH, Walters EH, Coleridge J, Maclean A, Thomson G. Presentation at the Thoracic Society of Australia and New Zealand meeting, Wellington, New Zealand, March 1997

13. "The Involvement of β_2-Agonists in Asthma Deaths"
Couper FJ. Presentation at the Victorian Institute of Forensic Medicine, Melbourne, Australia, March 20, 1997

14. "Postmortem Interpretation of β_2-Agonist Concentrations"
Couper FJ. Presentation at The International Association of Forensic Toxicologists 35th meeting, Padova, Italy, August 25, 1997

*15. "The Involvement of β_2-Agonists in Asthma-Related Deaths"
Couper FJ. Lecture at the Department of Respiratory Medicine & The Inner and Eastern Health Care Network, Respiratory Conference, Melbourne, Australia, November 4, 1997

16. "The Application of Hair Analysis to Detect Anabolic Steroid Use in Humans"
Couper FJ. Presentation at the Victorian Institute of Forensic Medicine, Melbourne, Australia, August 20, 1998

17. "The Role of β_2-Agonists in Asthma Deaths"
Couper FJ. Presentation at the Washington State Toxicology Laboratory, WA, U.S.A., September 18, 1998

18. "The Application of Hair Analysis to Detect Anabolic Steroid Use in Humans"
Couper FJ, Drummer OH. Presentation at the 14th International Symposium on the Forensic Sciences meeting, Adelaide, Australia, October 1998

19. "Blood Salbutamol Levels are Higher in Asthma Deaths than Controls after Adjusting for Administration and Severity"
Abramson M, Bailey M, **Couper F**, Drummer O, Forbes A, McNeil J, Walters EH. Presentation at the World Asthma Meeting, Barcelona, Spain, December 11, 1998

20. "Date Rape: How Often Are Drugs Found?"
Couper FJ. Training Seminar for the Madigan Army Medical Center and University of Washington Emergency Medicine Residency, Emergency Medicine Grand Rounds: Medical Toxicology, University of Washington, WA, U.S.A., January 13, 1999

21. "The Involvement of β_2-Agonists in Asthma Deaths"
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Orlando FL, February 18, 1999

*22. "Date Rape Drugs"
Couper FJ. Training Seminar for the Wahkiakum County Prosecuting Attorney's Office, Cathlamet, WA, U.S.A., June 17, 1999

23. "The Determination of GHB in Clinical and Postmortem Specimens"
Couper FJ. Presentation at the Society of Forensic Toxicologists meeting, San Juan PR, October 15, 1999

24. "Pharmacological Facilitation of Robbery: Analysis of Two Cases from the Emergecy Department"

Blaho KE, Park LJ, Logan BK, **Couper F**, Winbery SL. Presentation at the Society of Forensic Toxicologists meeting, San Juan PR, October 15, 1999

25. "Drug Facilitated Sexual Assaults"
Couper FJ. Presentation at the Washington State Toxicology Laboratory, WA, U.S.A., November 23, 1999

26. "Interpretation of GHB Concentrations in Clinical and Postmortem Specimens"
Couper FJ. Presentation at the Washington State Toxicology Laboratory, WA, U.S.A., November 23, 1999

27. "Toxicology of Heroin-Related Deaths"
Couper FJ. Presentation at the Preventing Heroin Overdose: Pragmatic Approaches Conference, Sheraton Towers, Seattle, WA, U.S.A., January 14, 2000

*28. "Medical Advocacy for Sexual Assault Victims: Rape Facilitating Drugs"
Couper FJ. Training Seminar for the Washington Coalition of Sexual Assault Programs, Olympia, WA, U.S.A., February 10, 2000

29. "The Prevalence of Drug Use in Tractor-Trailer Drivers: "Operation Trucker Check""
Couper FJ. Presentation at the Washington State Toxicology Laboratory, WA, U.S.A., February 17, 2000

30. "Zolpidem and Driving Impairment"
Logan BK, **Couper FJ**. Presentation at the American Academy of Forensic Sciences meeting, Reno NV, February 24, 2000

31. "Determination of Drug Use in Tractor-Trailer Drivers: "Operation Trucker Check""
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Reno NV, February 25, 2000

*32-35. "Women and Domestic Violence: Evidence Collection and the Crime Scene – Emphasis on Domestic Violence and Sexual Assault"
Couper FJ. Four Training Seminars for the Violence Against Women Act Stop Grant, Seattle, Bellevue and Kent, WA, U.S.A., April-May 2000

*36. "Recognition of Drug-Facilitated Sexual Assault"
Couper FJ. Training Seminar for student-advocates at Pacific Lutheran University, Tacoma, WA, U.S.A., April 28, 2000

*37. "Recognition of Drug-Facilitated Sexual Assault"
Couper FJ. Training Seminar for the Puget Sound Sexual Assault Centre, Tacoma, WA, U.S.A., June 21, 2000

38. "Drugs and Driving at the State Toxicology Laboratory"
Couper FJ. DRE Field In-Service Training Seminar, Evergreen State College, Olympia, WA, July 11, 2000

*39. "GHB and Date Rape Drugs"
Couper FJ. Lecture at the King County Medical Examiners Office, Seattle, WA, July 19, 2000

*40. "GHB and Driving Impairment"
Couper FJ. Presentation at the International Consultative Meeting on Drugs and Driving Impairment, Seattle, WA, July 31, 2000

*41. "Advances in Toxicology: Date Rape Drugs – Washington State Experience"
Couper FJ. Presentation at the Harborview Center for Sexual Assault and Traumatic Stress - Emergency Department Update: Acute Care for Sexual Assault Patients conference, Seattle, WA, September 26, 2000

42. "Driving Under the Influence of GHB"
Couper FJ. Presentation at the Society of Forensic Toxicologists meeting, Milwaukee WI, October 4, 2000

*43. "Forensic Services in Washington State"
Couper FJ. Training Seminar for the Northwest Medical Laboratory Symposium 2000, Tacoma WA, October 19, 2000

*44. "Recognizing Drug-Facilitated Sexual Assault"
Couper FJ. Training Seminar for the Seattle Police Department - Special Assault Unit, Seattle WA, October 25, 2000

*45. "Drug-Facilitated Sexual Assault – Washington State Experience"
Couper FJ. Training Seminar for the King County Prosecutors Office, Seattle WA, October 26, 2000

*46. "Analytical Methodologies for MDMA"
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Seattle WA, February 19, 2001

47. "Case Reports of Drivers Impaired by MDMA"
Logan BK, **Couper FJ**. Presentation at the American Academy of Forensic Sciences meeting, Seattle WA, February 19, 2001

48. "Effects of Drugs on Human Performance – Fact Sheets"
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Seattle WA, February 20, 2001

*49. "General Analytical Approaches to DFSA in Washington State"
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Seattle WA, February 20, 2001

50. "Suspected GHB Overdoses in the Emergency Room"
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Seattle WA, February 21, 2001

*51. "Street Drug Scene Update: A Toxicologist's View"
Couper FJ. Presentation at the 14th Annual Northwest Conference on Addictions, Seattle WA, May 2, 2001

*52. "Advances in Toxicology: Date Rape Drugs"
Couper FJ. Presentation at the Conference on Acute Care for Sexual Assault Patients: Advances in Diagnosis, Treatment, and Forensic Investigation, Yakima WA, May 17, 2001

53. "Addicted to DUI – a GHB / GBL Case Report"
Couper FJ. Presentation at the Society of Forensic Toxicologists meeting, New Orleans LA, October 3, 2001

*54. "How do we know that a person's use of prescription and O-T-C medications affects their ability to operate a motor vehicle?"
Couper FJ. Presentation at the National Transportation Safety Board - Food and Drug Administration Joint Public Meeting, Washington DC, November 14, 2001

55. "GHB: Use and Abuse"
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Atlanta GA, February 11, 2002

56. "CNS Depressants: Is this Driver Impaired by Drugs?"
Couper FJ. Presentation at the American Academy of Forensic Sciences meeting, Atlanta GA, February 12, 2002

*57. "Selected CNS Depressant Drugs and Their Effects on Driving"
Couper FJ. Presentation at the inaugural Robert F. Borkenstein Center for Studies of Law in Action course on The Effects of Drugs on Human Performance and Behavior, Bloomington IN, March 25, 2002

*58. "GHB: Use and Abuse"
Couper FJ. Presentation at the Armed Forces Institute of Pathology, Rockville MD, April 25, 2002

59. "The Role of Toxicology in Death Investigations"
Couper FJ. Presentation at the Homicide School, Washington DC, June 6, 2002

60. "The Role of Toxicology in Death Investigations"
Couper FJ. Presentation at the Homicide School, Washington DC, February 11, 2003

*61. "Selected CNS Depressant Drugs and Their Effects on Driving"
Couper FJ. Presentation at the Robert F. Borkenstein Center for Studies of Law in Action course on The Effects of Drugs on Human Performance and Behavior, Bloomington IN, March 17-18, 2003

*62. "Hallucinogens"
Couper FJ. Presentation at the FBI Laboratory Symposium on Forensic Toxicology. Washington DC, August 28-29, 2004

*63. "CNS Depressant Drugs and Human Performance"
Couper FJ. Presentation at the Robert F. Borkenstein Center for Studies of Law in Action course on The Effects of Drugs on Human Performance and Behavior, Bloomington IN, September 20-22, 2004

*64. "Interpretive Toxicology & Drug Impaired Driving"
Couper FJ. Instructor at the Drug Impaired Driving Workshop, The Arizona DPS Crime Laboratory, Phoenix, AZ, November 29 – December 3, 2004

65. "The Role of the Toxicology Laboratory in DUI Cases"
Couper FJ. Presentation at the D.C. United DWI Training (O.A.G., M.P.D., U.S.C.P., U.S.P.P., U.S.S.S., F.B.I), Washington DC, May 20, 2005

*66. "Drug-Facilitated Sexual Assaults"
Couper FJ. Presentation to the U.S. Attorney's Office, Metropolitan Police Department and U.S. Park Police sexual assault investigators, Washington DC, June 28, 2005

*67. "Introduction to Drugged Driving"
Couper FJ. Presentation at the combined SFST Training (U.S.P.P. and M.P.D.), Bolling Airforce Base, Washington DC, March 29, 2007

*68. "The Role of Toxicology in DUI Investigations"
Couper FJ. Presentation at the D.C. Attorney General Court Training (O.A.G., M.P.D., U.S.S.S.), Washington DC, December 6, 2007

69. "WSP State Toxicology Laboratory Division update"
Couper FJ, Jones KE. Presentation at the WAPA District Court Training, Leavenworth WA, May 28, 2008